CHAPTER 4

Conjunctiva

Introduction

Applied anatomy

Subdivisions

1. **Palpebral** starts at the mucocutaneous junction of the lid margins and is firmly adherent to the tarsal plates.
2. **Forniceal** is loose and redundant so that it swells easily and may be thrown into folds.
3. **Bulbar** covers the anterior sclera. The stroma of the bulbar conjunctiva is loosely attached to the underlying Tenon capsule, except at the limbus, where the attachment is firm.

Histology

1. **The conjunctival epithelium** is between two and five cell layers thick. Basal cuboidal cells evolve into flattened polyhedral cells as they reach the surface. With chronic exposure and drying, the epithelium may become keratinized.
2. **The stroma** (substantia propria) consists of richly vascularized connective tissue, separated from the epithelium by a basement membrane. The adenoid superficial layer does not develop until about 3 months after birth, hence the inability of the newborn to produce a follicular conjunctival reaction. The deep, thicker fibrous layer is continuous with the tarsal plates and belongs to the subconjunctival tissues rather than the conjunctiva.

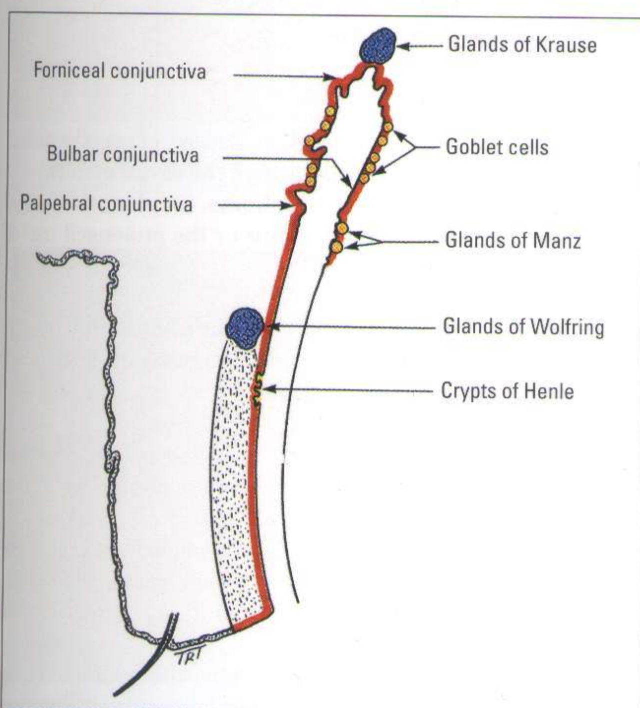


Fig. 4.1
Anatomy of the conjunctiva and its glands

Glands

1. **Mucin secretors** (Fig. 4.1)
   a. ***Goblet cells***, located within the epithelium, are most dense inferonasally.
   b. ***Crypts of Henle*** are located along the upper third of the superior tarsal conjunctiva and along the lower third of the inferior tarsal conjunctiva.
   c. ***Glands of Manz*** encircle the limbus.

> ***NB:*** Destructive disorders of the conjunctiva such as cicatricial pemphigoid frequently damage the mucin secretors, whereas chronic inflammatory disorders may be associated with an increase in number of goblet cells.

2. **Accessory lacrimal glands** of Krause and Wolfring are located deep within the substantia propria.

Clinical evaluation

Clinical features relevant to the differential diagnosis of conjunctival inflammation are: (a) *symptoms*, (b) *discharge*, (c) *conjunctival reaction*, (d) *membranes* and (e) *lymphadenopathy*.

Symptoms

1. **Non-specific** symptoms include lacrimation, irritation, stinging, burning and photophobia.
2. **Pain** and foreign body sensation suggest associated corneal involvement.
3. **Itching** is the hallmark of allergic conjunctivitis although it may also occur in blepharitis and keratoconjunctivitis sicca.

Discharge

This is composed of the exudate that has filtered through the conjunctival epithelium from dilated blood vessels. On the surface of the conjunctiva, variable amounts of epithelial debris, mucus and tears are added. The discharge can range from watery through mucopurulent to grossly purulent.

1. **A watery** discharge is composed of a serous exudate and a variable amount of reflexly secreted tears. It is typical of acute viral and acute allergic inflammations.
2. **A mucoid** discharge is typical of vernal conjunctivitis and keratoconjunctivitis sicca.
3. **A purulent** discharge occurs in severe acute bacterial infections.
4. **A mucopurulent** discharge occurs in mild bacterial as well as chlamydial infections.

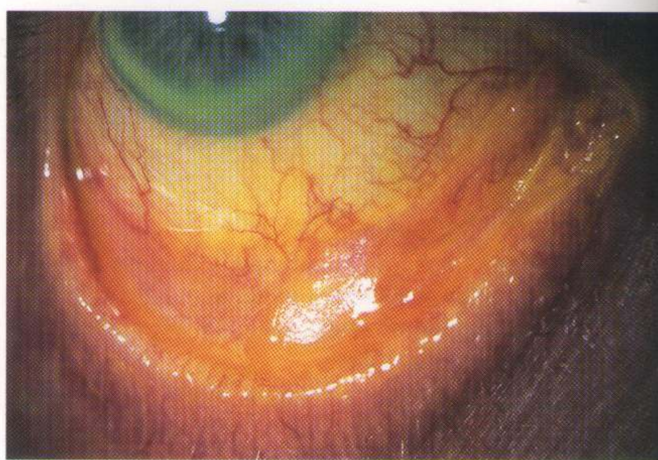
Conjunctival reaction

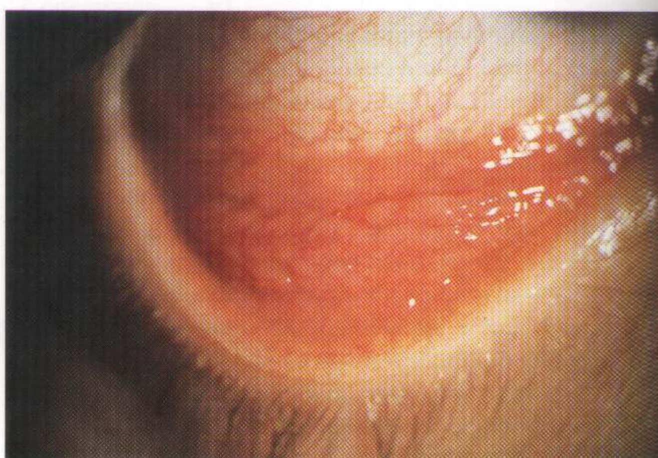
1. **Conjunctival injection** is frequently maximal in the fornices. A velvety, beefy-red conjunctiva suggests a bacterial aetiology (Fig. 4.2).
2. **Subconjunctival haemorrhages** usually occur with viral infections although they may be present with bacterial infections with *Strep. pneumoniae* and *H. aegypticus* (Fig. 4.3).


Fig. 4.2
Conjunctival injection in bacterial infection


Fig. 4.3
Subconjunctival haemorrhage


Fig. 4.4
Severe chemosis


Fig. 4.5
Conjunctival scarring


Fig. 4.6
Conjunctival follicles

3. **Oedema** (chemosis) may occur when the conjunctiva is severely inflamed. Exudation of protein-rich fluid through the walls of the inflamed blood vessels produces a translucent swelling. Large redundant folds may form in the fornices (Fig. 4.4) and in severe cases chemotic conjunctiva may protrude through the closed eyelids.
4. **Scarring** may indicate trachoma, ocular cicatricial pemphigoid, atopic conjunctivitis or the prolonged use of topical medication (Fig. 4.5).
5. **Follicular reaction**
   a. *Composition.* Follicles are subepithelial foci of hyperplastic lymphoid tissue within the stroma associated with accessory vascularization.
   b. *Signs* (Fig. 4.6)
      - Multiple, discrete, slightly elevated lesions reminiscent of small grains of rice, most prominent in the fornices.
      - Each follicle is encircled by a tiny blood vessel and the size of each lesion, which can vary from 0.5 to 5 mm, is related to the severity and duration of the inflammation.
      - As the follicle increases in size, the accompanying vessels are displaced peripherally, eventually appearing as a vascular capsule enclosing the base of the follicle.

c. *Causes* include viral and chlamydial infections, Parinaud oculoglandular syndrome and hypersensitivity to topical medication.

> *NB:* Asymptomatic follicles in children (folliculosis) have no clinical significance.

6. **Papillary reaction** is non-specific and therefore of less diagnostic value than a follicular response.
   a. *Composition*
      - Hyperplastic conjunctival epithelium thrown into numerous folds or projections, with central vessels and a diffuse infiltrate of chronic inflammatory cells, including lymphocytes, plasma cells and eosinophils.
      - Papillae can develop only in the palpebral conjunctiva and the bulbar conjunctiva at the limbus, where the conjunctival epithelium is attached to the underlying structures by fibrous septa.
   b. *Signs* (Fig. 4.7)
      - Papillae are most frequently seen in the upper palpebral conjunctiva as a fine mosaic-like pattern of elevated polygonal hyperaemic areas separated by paler channels.
      - The central fibrovascular core produces a glomerulus-like appearance on reaching the surface.
      - With prolonged inflammation, the fibrous septa which anchor the papillae to the underlying tissues may rupture, leading to confluence and increase in size.
      - Late changes include superficial stromal hyalinization and formation of crypts containing goblet cells between the papillae.

> *NB:* The appearance of the normal superior edge of the tarsal plate (inferior when everted) may mimic papillae and follicles and should therefore not be used as a clinical sign (Fig. 4.8).

   c. *Causes* include chronic blepharitis, allergic and bacterial conjunctivitis, contact lens wear, superior limbic keratoconjunctivitis and floppy eyelid syndrome.


Fig. 4.7
Conjunctival papillae (Courtesy of C. Barry)


Fig. 4.8
Normal appearance of the medial aspect of the upper palpebral conjunctiva

Membranes

1. **Pseudomembranes** consist of coagulated exudate adherent to the inflamed conjunctival epithelium. Characteristically, they can be easily peeled off, leaving the epithelium intact (Fig. 4.9). Causes include severe adenoviral and gonococcal infection, ligneous conjunctivitis and Stevens–Johnson syndrome.
2. **True membranes** infiltrate the superficial layers of the conjunctival epithelium. Attempts to remove the membrane may be accompanied by tearing of the epithelium and bleeding. The main causes are infections resulting from *Strep. pyogenes* and diphtheria.

Lymphadenopathy

Lymphatic drainage of the conjunctiva is to the preauricular and submandibular nodes, which corresponds to the drainage of the eyelids (*see* Fig. 1.3). The main causes of lymphadenopathy are viral, chlamydial and gonococcal infections and Parinaud oculoglandular syndrome.


Fig. 4.9
Removal of a conjunctival pseudomembrane (Courtesy of J. Dart)

Laboratory investigations

Indications

1. **Severe purulent conjunctivitis**: to identify pathogens and institute appropriate antimicrobial therapy based on sensitivity.
2. **Follicular conjunctivitis**: to differentiate viral from early chlamydial infection.
3. **Conjunctival inflammations**, in which the clinical picture is insufficiently distinctive to suggest an aetiological diagnosis.
4. **Neonatal conjunctivitis**.

Specific investigations

1. **Cultures** are now rarely performed as they have been replaced by more accurate and quicker techniques.
2. **Cytological investigation**, based on the presence of characteristic cellular infiltrates, is insensitive and subjective.
3. **Inoculation** of susceptible cell lines and observation of cytopathic effect or visualization with various chemical and immunological staining techniques.
4. **Detection of viral or chlamydial antigens** in conjunctival and corneal specimens.
5. **Impression cytology** in which a piece of cellulose acetate filter paper is pressed against the conjunctiva or cornea. Surface epithelial cells adhere to the paper when removed and can be examined microscopically. This may be useful in the diagnosis of ocular surface neoplasia, dry eyes, ocular cicatricial pemphigoid, limbal stem cell failure and infections.
6. **Polymerase chain reaction** (PCR) allows the speedy identification of extremely small quantities of DNA with a very high degree of specificity. It is useful for the detection of adenovirus, herpes simplex and *Chlamydia trachomatis* in conjunctival swabs.

Bacterial infections

Simple bacterial conjunctivitis

Simple bacterial conjunctivitis is a common and usually self-limiting condition which most commonly affects children. The most frequent causative organisms are *Staph. epidermidis*, *Staph. aureus*, *Strep. pneumoniae* and *H. influenzae*. Spread of the infection is usually the result of direct contact with infected secretions.

Clinical features

1. **Presentation** is with acute redness, grittiness, burning and discharge. On waking, the eyelids are frequently stuck together and difficult to open as a result of the accumulation of exudate during the night. Both eyes are usually involved, although one may become affected before the other by a day or so.
2. **Signs**
   - The eyelids are crusted and may be oedematous (Fig. 4.10).
   - The discharge is initially watery (Fig. 4.11), mimicking viral conjunctivitis, but within a day or so it becomes mucopurulent (Fig. 4.12). Mucous strands may develop in the inferior fornix.
   - Injection is maximal in the fornices and least at the limbus.
   - The tarsal conjunctiva has a velvety, beefy-red appearance and shows mild papillary changes.
   - Superficial punctate epithelial erosions are frequent but innocuous.

Treatment

Even without treatment, simple conjunctivitis usually resolves within 10–14 days and laboratory tests are not routinely performed. Before initiating treatment, it is



Fig. 4.10
Severe crusting of the eyelids in bacterial conjunctivitis



Fig. 4.11
Watery discharge



Fig. 4.12
Mucopurulent discharge in bacterial conjunctivitis

important to clean the eyelids and lashes of discharge. Broad-spectrum antibiotics should be administered in drop form during waking hours and as ointment at bedtime until the discharge has ceased.

1. **Antibiotic drops**
   a. ***Fusidic acid*** (Fucithalmic) is a viscous suspension which is useful for staphylococcal infections but not for most Gram-negative bacteria. Initial treatment is q.i.d. for 48 hours and then b.d.
   b. ***Chloramphenicol*** has a broad spectrum and is initially administered every 1–2 hours.
   c. ***Other antibiotics*** in drop form currently available include: ciprofloxacin, ofloxacin, lomefloxacin, gentamicin, neomycin, framycetin, tobramycin, Neosporin (polymyxin B + neomycin + gramicidin) and Polytrim (polymyxin + trimethoprim).
2. **Antibiotic ointments** provide higher concentrations for longer periods than drops, but use during the day is limited because they cause blurred vision. However, ointments can be used at night to provide a good concentration of antibiotic during sleep. Antibiotics available in ointment form include chloramphenicol, gentamicin, tetracycline, framycetin, Polyfax (polymyxin B + bacitracin) and Polytrim.

Gonococcal keratoconjunctivitis

Gonorrhoea is a venereal genitourinary tract infection caused by the Gram-negative diplococcus *Neisseria gonorrhoeae*, which is capable of invading the intact corneal epithelium.

Conjunctivitis

1. **Presentation** is with acute conjunctival discharge.
2. **Signs**
   - The eyelids are oedematous and tender.
   - The discharge is profuse and purulent (Fig. 4.13).
   - Intense conjunctival hyperaemia, chemosis and frequently pseudomembrane formation (Fig. 4.14).
   - Lymphadenopathy is prominent and, in severe cases, suppuration may occur.



Fig. 4.13
Purulent discharge in gonococcal conjunctivitis



Fig. 4.14
Conjunctival pseudomembranes

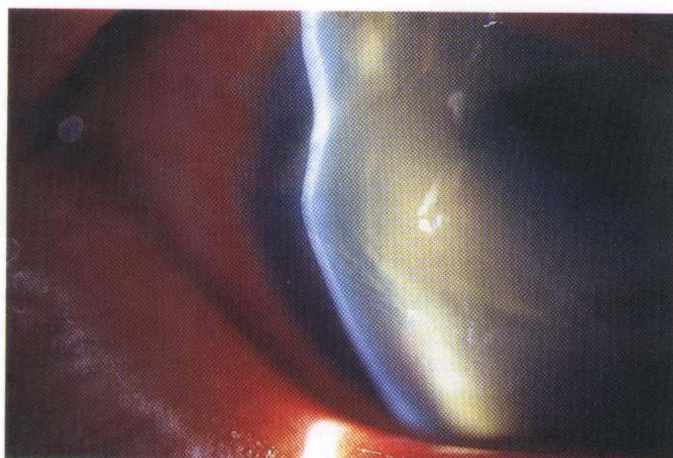


Fig. 4.15
Corneal ulceration in gonococcal infection



Fig. 4.16
Corneal perforation and endophthalmitis in gonococcal infection

Keratitis

Unless conjunctivitis is treated promptly keratitis may occur and progress as follows:

- Marginal ulceration in the pus filled sulcus between the chemosed conjunctiva and the cornea at the limbus.
- Coalescence to form a peripheral ring ulcer.
- Central ulceration (Fig. 4.15) which may rapidly lead to perforation and endophthalmitis (Fig. 4.16).

Treatment

The patient should be hospitalized, cultures taken and the discharge removed at frequent intervals.

1. **Systemic** treatment is with cefotaxime 1 g intravenously b.d. If only the conjunctiva is involved 1 day's treatment may suffice, but corneal involvement may necessitate treatment for longer.
2. **Topical** gentamicin or bacitracin initially at very frequent intervals.

NB: It is important to recognize and treat any associated chlamydial infection.

Viral infections

Adenoviral keratoconjunctivitis

The spectrum of adenoviral eye infection varies from mild and almost inapparent disease to full-blown infection with significant morbidity. It is an occupational hazard of ophthalmologists. Transmission of this highly contagious virus is via respiratory or ocular secretions, and dissemination is by contaminated towels or equipment such as tonometer heads. The incubation period is 4–10 days. Following the onset of conjunctivitis the virus is shed for about 12 days. Precautions must be taken to avoid transmission following examination of patients with suspected adenovirus infection. Thorough washing of hands is most important, as is meticulous disinfection of ophthalmic instruments. In addition, infected hospital personnel should not come in contact with patients.

Causative viruses

1. **Pharyngoconjunctival fever (PCF)** is most frequently caused by adenovirus types 3, 4 and 7 and occasionally type 5. It is transmitted by droplets and typically affects children who also develop an upper respiratory tract infection. Keratitis develops in about 30% of cases but is seldom severe.
2. **Epidemic keratoconjunctivitis (EKC)** is most frequently caused by adenovirus types 8 and 19, but several other types may also be responsible. The infection is transmitted by hand to eye contact, instruments and solutions. In contrast to PCF it does not cause systemic symptoms. Keratitis, which may be severe, develops in about 80% of cases.



Fig. 4.17
Eyelid oedema in adenoviral infection



Fig. 4.18
Conjunctival follicles in adenoviral infection

Conjunctivitis

1. **Presentation** is with acute watering, redness, discomfort and photophobia frequently involving both eyes.
2. **Signs**
   - Eyelid oedema (Fig. 4.17).
   - Watery discharge and conjunctival follicles (Fig. 4.18).
   - Subconjunctival haemorrhages, chemosis and pseudomembranes (Fig. 4.19) in severe cases.
   - Tender lymphadenopathy.
3. **Treatment** is largely symptomatic and supportive. Spontaneous resolution occurs within 2 weeks. Antiviral agents are ineffective and topical steroids should be avoided unless the inflammation is very severe.

Keratitis

1. **Signs**
   a. Stage 1 occurs within 7–10 days of the onset of symptoms and is characterized by a punctate epithelial keratitis which resolves within 2 weeks (Fig. 4.20).
   b. Stage 2 is characterized by focal, white, subepithelial opacities which develop beneath the fading epithelial lesions (Fig. 4.21). They are thought to represent immune response to the virus and may be associated with mild transient anterior uveitis.
   c. Stage 3 is characterized by anterior stromal infiltrates which gradually fade over months or years (Fig. 4.22).
2. **Treatment** with topical steroids is indicated only if the eye is uncomfortable or visual acuity diminished by stage 3 lesions. Steroids do not shorten the natural course of the disease but merely suppress the corneal inflammation so that the lesions tend to recur if steroid therapy is discontinued prematurely.



Fig. 4.19
Conjunctival pseudomembranes in adenoviral infection



Fig. 4.20
Punctate epithelial keratitis in stage 1 adenoviral infection



Fig. 4.21
Subepithelial opacities in stage 2 adenoviral infection



Fig. 4.22
Anterior stromal opacities in stage 3 adenoviral infection

Molluscum contagiosum conjunctivitis

Molluscum is an oncogenic virus that produces characteristic lesions on the skin and, less commonly, on mucous membranes. Spread is by close contact. The condition typically affects adolescent children and young adults. Molluscum is also a common finding in patients with AIDS, in whom multiple lesions may develop. Patients with ocular involvement may also manifest mollusca involving other parts of the body.

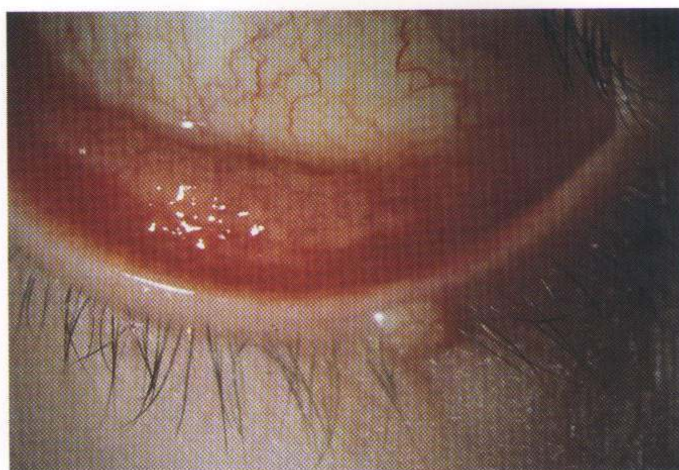


Fig. 4.23
Follicular conjunctivitis associated with a solitary molluscum lesion on the lower lid margin

1. **Signs**
   - The lid margin shows a small, pale, waxy, umbilicated nodule.
   - The lesion may be missed if atypical in appearance or some distance from the lid margin.
   - The discharge is usually mild and mucoid.
   - The conjunctiva shows a follicular response ipsilateral to the lid lesion (Fig. 4.23).
   - Rarely, immunocompromised patients may develop molluscum nodules on the bulbar conjunctiva.
   - Long-standing cases may develop fine epithelial keratitis which may progress to pannus formation if untreated.
2. **Treatment** involves destruction of the lid lesion by expression, shave excision, cryotherapy or cauterization.

Chlamydial infections

Adult chlamydial conjunctivitis

Adult chlamydial conjunctivitis is a sexually transmitted disease caused by serotypes D to K *Chlamydia trachomatis*. Patients with chlamydial conjunctivitis are generally young and many have a concomitant genital infection (cervicitis in women and urethritis in men) which may be asymptomatic (*see* Chapter 20). Transmission is by autoinoculation from genital secretions although eye-to-eye spread may occur. The incubation period is about 1 week.

Clinical features

1. **Presentation** is with a subacute onset of unilateral or bilateral mucopurulent discharge. Unlike adenoviral infection, the conjunctivitis becomes chronic and may persist for 3–12 months if untreated.
2. **Signs**
   - Scant mucopurulent discharge.
   - Large follicles, most prominent in the inferior forniceal conjunctiva (Fig. 4.24), which may also involve the upper tarsal conjunctiva (Fig. 4.25).
   - Peripheral corneal infiltrates may appear 2–3 weeks after the onset of conjunctivitis (Fig. 4.26).
   - Tender lymphadenopathy.

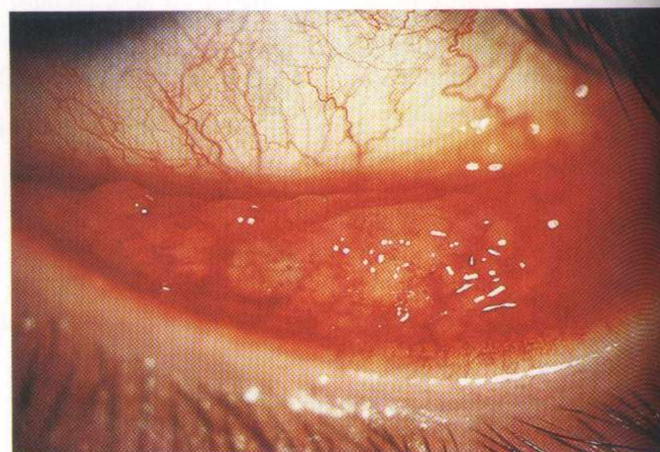


Fig. 4.24
Large conjunctival follicles in adult chlamydial infection



Fig. 4.25
Conjunctival follicles in adult chlamydial infection

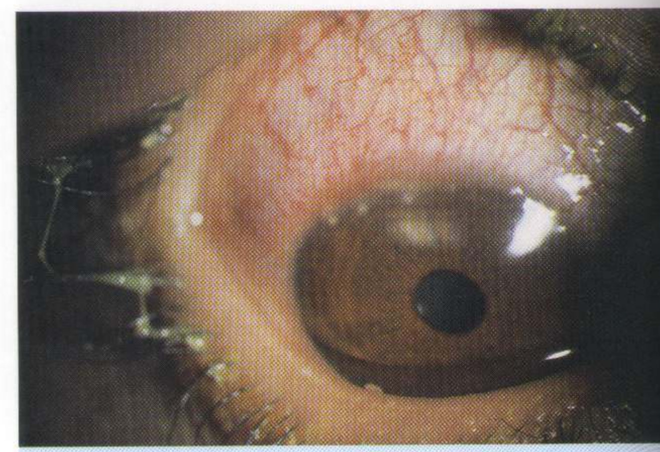


Fig. 4.26
Marginal infiltrates in adult chlamydial infection

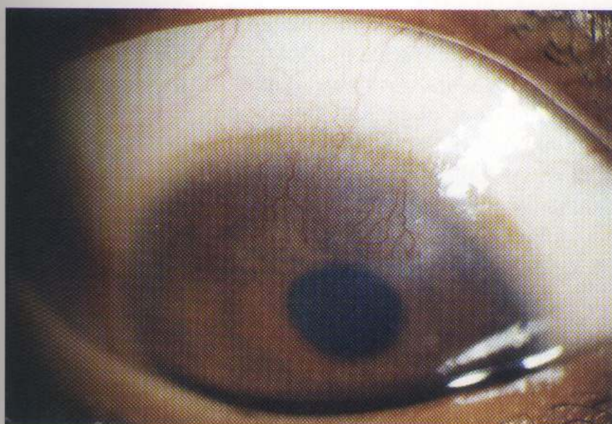


Fig. 4.27
Superior micropannus in long-standing adult chlamydial infection

- Long-standing cases are characterized by less prominent follicles and the development of mild conjunctival scarring and a superior pannus (Fig. 4.27).

Laboratory investigations

Confirmation of clinical diagnosis can be achieved through laboratory tests. In view of the venereal nature of the disease, referral to a genitourinary clinic is mandatory for investigation and management of other possible sexually transmitted diseases. Currently used tests include:

1. **Direct monoclonal fluorescent antibody microscopy** of conjunctival smears, which is rapid and inexpensive.
2. **Enzyme-linked immunosorbent assay** for chlamydial antigens.
3. **Standard single-passage McCoy cell culture**, which requires at least 3 days.
4. **Polymerase chain reaction.**

Treatment

1. **Topical** treatment is with tetracycline ointment q.i.d. for 6 weeks.
2. **Systemic** therapy is with one of the following:
   - Azithromycin 1 g as a single dose.
   - Doxycycline 100 mg b.d. for 1–2 weeks.
   - Erythromycin 500 mg q.i.d. for 1 week if tetracycline is inappropriate.

> *NB:* It is essential that sexual partners are identified and treated.

Neonatal chlamydial conjunctivitis

Chlamydial infection is the most common cause of neonatal conjunctivitis and is notifiable. It may be associated with systemic chlamydial infection which may result in otitis, rhinitis and pneumonitis. Because the infection is transmitted from the mother during delivery it is important that both parents are examined for evidence of genital infection.



Fig. 4.28
Mucopurulent discharge in neonatal chlamydial infection

1. **Presentation** is usually 5–19 days after birth.
2. **Signs**. Mucopurulent discharge (Fig. 4.28) and a papillary conjunctival reaction because infants cannot form follicles until about the third month of life. Occasional complications, if untreated, include conjunctival scarring and superior corneal pannus.
3. **Treatment** is with topical tetracycline and oral erythromycin ethyl succinate 25 mg/kg body weight b.d. for 2 weeks.

> *NB:* Systemic tetracycline is contraindicated in children under the age of 12 as well as pregnant or breast-feeding women because it may cause dental staining and occasionally hypoplasia in offspring.

Trachoma

Trachoma is an infection caused by serotypes A, B, Ba and C of *Chlamydia trachomatis*. It is a disease of underprivileged populations with poor conditions of hygiene. The common fly is the major vector in the infection–reinfection cycle. Currently trachoma is the leading cause of preventable blindness in the world.

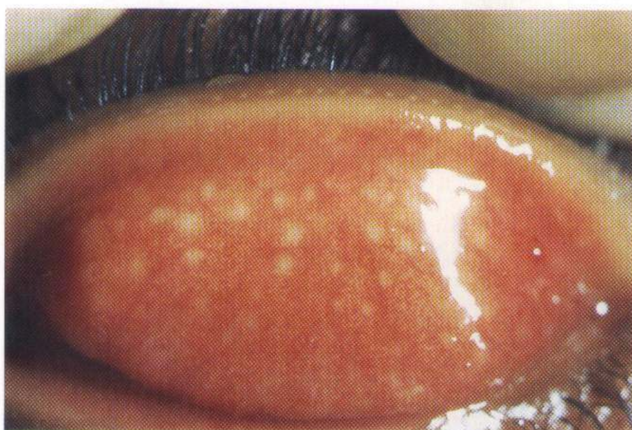


Fig. 4.29
Conjunctival follicles and papillae in early active trachoma

Clinical features and treatment

1. **Presentation** is during childhood with a mixed follicular/papillary conjunctivitis (Fig. 4.29). In children under the age of 2 years the papillary component may predominate.

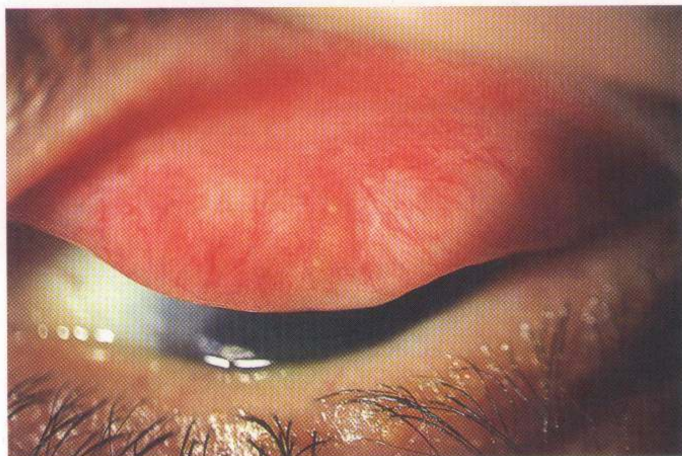


Fig. 4.30
Mild conjunctival scarring in chronic trachoma

2. **Chronic conjunctival inflammation** results in fine linear or stellate scars in milder cases (Fig. 4.30), or broad confluent scars (Arlt lines) (Fig. 4.31) in severe cases. The entire conjunctiva is involved but the effects are most prominent on the upper tarsus.
3. **Limbal follicles** are a unique feature. They later cicatrize and become covered by epithelium, resulting in an uneven surface (Herbert pits) (Fig. 4.32).
4. **Keratitis**, during the inflammatory stage, ranges from superior epithelial keratitis to anterior stromal infiltrates and pannus formation (Fig. 4.33).
5. **Progressive conjunctival scarring**, if severe, causes distortion of the eyelids, particularly of the upper tarsus (Fig. 4.34), to produce trichiasis (Fig. 4.35) and cicatricial entropion (Fig. 4.36). It may also destroy conjunctival goblet cells and involve the ductules of the lacrimal gland, resulting in a dry eye.
6. **End-stage trachoma** is characterized by severe corneal ulceration and opacification.
7. **Treatment** is with a single dose of azithromycin 1 g. The most important preventive measure is strict personal hygiene.

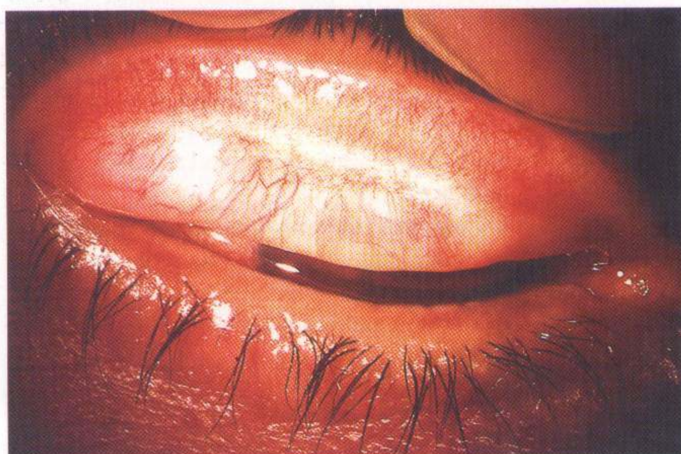


Fig. 4.31
Conjunctival scarring (Arlt line) in chronic trachoma

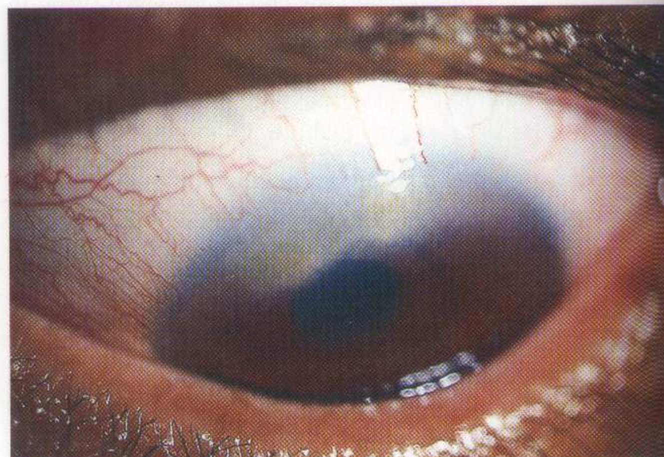


Fig. 4.33
Trachomatous pannus



Fig. 4.32
Herbert pits in trachoma

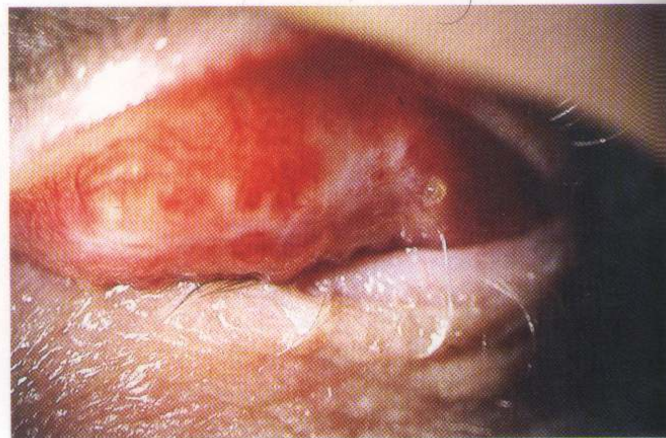


Fig. 4.34
Severe conjunctival scarring in trachoma


Fig. 4.35
Trichiasis and corneal vascularization in advanced trachoma


Fig. 4.36
Entropion of the upper eyelid in advanced trachoma (Courtesy of C. Barry)

World Health Organization grading of trachoma

TF = trachoma follicles with five or more on the superior tarsus.
TI = trachomatous inflammation diffusely involving the tarsal conjunctiva, which obscures 50% or more of the normal deep tarsal vessels.
TS = trachomatous conjunctival scarring.
TT = trachomatous trichiasis touching the cornea.
CO = corneal opacity.

Allergic inflammations

Allergic rhinoconjunctivitis

Allergic rhinoconjunctivitis, the most common form of ocular and nasal allergy, is a hypersensitivity reaction to specific airborne antigens.


Fig. 4.37
Allergic rhinoconjunctivitis

1. **Classification**
   a. ***Seasonal allergic*** rhinoconjunctivitis, with onset of 'hay fever' during the summer, is the commonest and mildest form of allergic conjunctivitis. The most common allergens are pollens.
   b. ***Perennial allergic*** rhinoconjunctivitis causes symptoms throughout the year with exacerbation in the autumn when exposure to dust mites and fungal allergens is greatest. It is less prevalent and milder than the seasonal type but more persistent.
2. **Presentation** is with transient, acute attacks of redness, watering and itching, associated with sneezing and nasal discharge.
3. **Signs**
   - Lid oedema.
   - The conjunctiva has a milky (Fig. 4.37) or pinkish appearance as a result of oedema and injection.
   - Small papillae may occur on the upper tarsal conjunctiva.
4. **Treatment** is with either a topical mast cell stabilizer (nedocromil, lodoxamide) or a topical antihistamine (levocabastine, azelastine or emedastine) b.d. to q.i.d. when the patient is symptomatic. Otopatadine 0.1% is both an antihistamine and a mast cell stabilizer which is effective when used b.d. Lotepredol etabonate 0.5% q.i.d. may also be helpful.

Vernal keratoconjunctivitis

Vernal keratoconjunctivitis (VKC) is a recurrent, bilateral, external, ocular inflammation primarily affecting boys and young adults living in warm, dry climates. It is an allergic disorder in which IgE and cell-mediated immune mechanisms play an important role. About three-quarters of patients have associated atopy and two-thirds have a family history of atopy. Such patients often develop asthma and eczema in infancy. The onset of VKC is usually after the age of 5 years and the condition eventually resolves around puberty, only rarely persisting beyond the age of 25 years. VKC may

occur on a seasonal basis, with a peak incidence over late spring and summer, although many patients have year-round disease. Patients with VKC have a higher incidence of keratoconus as well as other types of corneal ectasia such as pellucid marginal degeneration and keratoglobus.

The main symptoms are intense ocular itching which may be associated with lacrimation, photophobia, foreign body sensation and burning. Thick mucus discharge and ptosis also occur. The three main clinical types are: (a) *palpebral*, (b) *limbal* and (c) *mixed*. Limbal signs are more common in dark-skinned races, while tarsal and corneal signs predominate in lighter-skinned races. It is, however, likely that many mild or atypical forms may be unrecognized because no precise diagnostic criteria have been established. The long-term prognosis is good.

Clinical features

1. **Palpebral VKC** (in chronological order)
   - Diffuse papillary hypertrophy, most marked on the superior tarsus (Fig. 4.38).
   - The papillae enlarge and have a flat-topped polygonal appearance reminiscent of cobblestones (Fig. 4.39).
   - In severe cases, the connective tissue septa rupture, giving rise to giant papillae, which may be coated by copious mucus (Fig. 4.40).
   - As the inflammation settles the papillae shrink and become more separated but often do not disappear.
2. **Limbal VKC** is characterized by mucoid nodules scattered around the limbus with discrete white superficial spots (Trantas dots) composed predominantly of eosinophils at the apices of the lesions (Fig. 4.41).

Keratopathy

This is common and may take the following forms:

1. **Punctate epithelial erosions** involving the superior cornea are the earliest findings.
2. **Shield ulceration** (Fig. 4.42) is a serious problem which may be complicated by bacterial keratitis and rarely perforation.

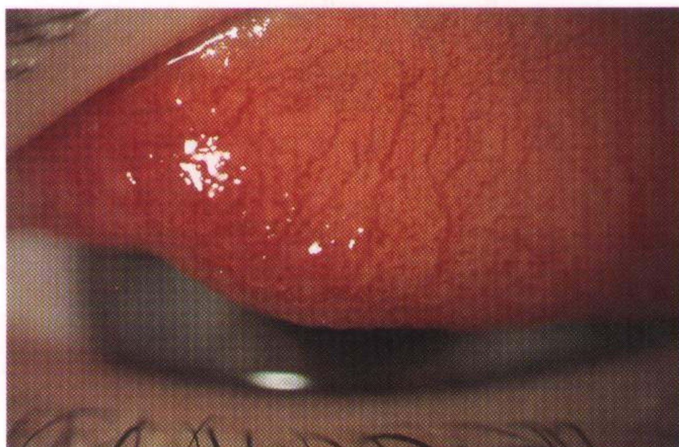


Fig. 4.38
Conjunctival hyperaemia and diffuse papillary hypertrophy in mild vernal disease



Fig. 4.40
Giant papillae and copious mucus in advanced vernal disease (Courtesy of A. Bacon)

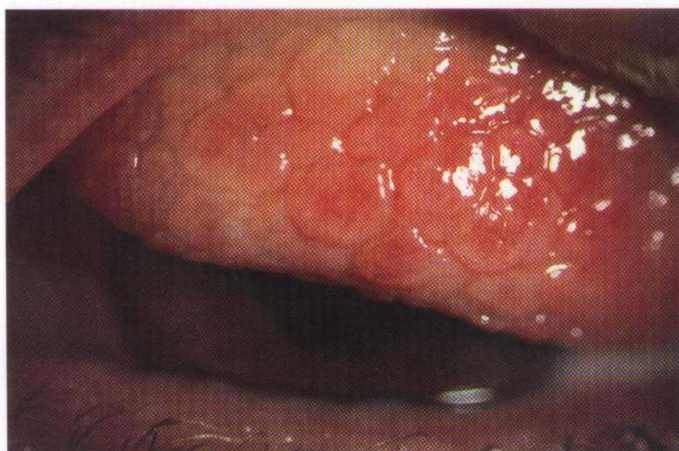


Fig. 4.39
'Cobblestone' papillae in severe vernal disease

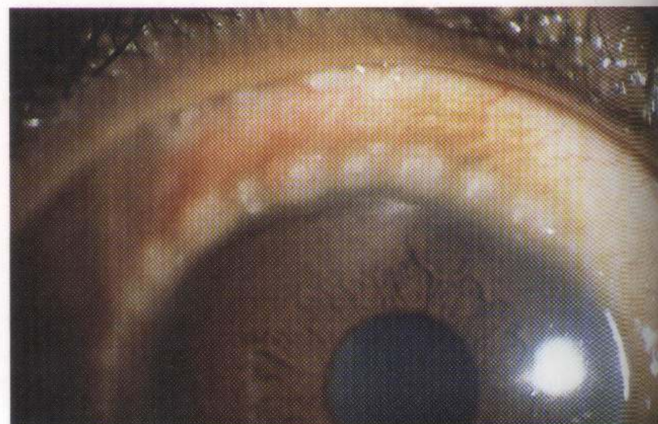


Fig. 4.41
Limbal nodules with overlying fine white plaques (Trantas dots) in vernal limbitis

3. **Plaque formation** (Fig. 4.43) may occur when the base of the ulcer becomes coated with desiccated mucus. This results in defective wetting by tears, prevents re-epithelialization and predisposes to subepithelial scarring and vascularization.
4. **Pseudogerontoxon** resembles an arcus senilis and is usually characterized by a 'cupid's bow' outline in a previously inflamed segment of the limbus (Fig. 4.44).

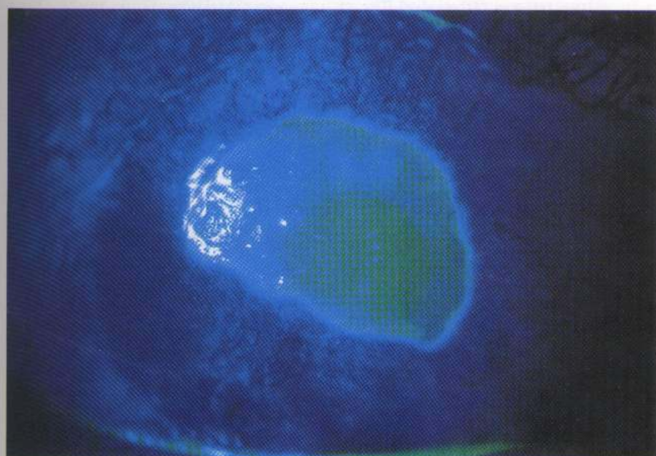


Fig. 4.42
Shield-like corneal ulceration stained with fluorescein in vernal disease (Courtesy of C. Barry)



Fig. 4.43
Corneal plaque in vernal disease



Fig. 4.44
Pseudogerontoxon in vernal disease

Treatment

1. **Topical**
   a. *Steroids* are indicated mainly for keratopathy although they may be required as short-term therapy for severe discomfort in patients with only conjunctival involvement. Fluorometholone should be used since it has a weaker ocular hypertensive effect than dexamethasone and prednisolone. It is often possible to discontinue steroids between attacks and treat exacerbations vigorously with high doses, tapering to a relatively small dose as quickly as possible.
   b. *Mast cell stabilizers* such as nedocromil b.d. and lodoxamide q.i.d. are used as prophylactic therapy that reduces the need for steroids. They do not have the side effects of steroids and can therefore be used for prolonged periods but are not effective in controlling acute exacerbations.
   c. *Antihistamines* such as levocabastine are also effective.
   d. *Acetylcysteine 0.5%* has mucolytic properties and is useful in the treatment of early plaque formation.
   e. *Cyclosporin 2%* may be useful in steroid-resistant cases but is not yet widely available.
2. **Supratarsal steroid injection** of betamethasone or triamcinolone is effective in patients with severe disease unresponsive to conventional therapy.
3. **Surgical** treatment may be required for severe shield ulcers resistant to medical therapy. This may involve debridement, superficial keratectomy, excimer laser phototherapeutic keratectomy as well as amniotic membrane transplantation to enhance re-epithelialization.

Atopic keratoconjunctivitis

Atopic keratoconjunctivitis (AKC) is a relatively rare, but potentially serious, condition which typically affects young men with atopic dermatitis (*see* Chapter 20). Patients with atopic dermatitis may develop ocular involvement several years after the onset of other atopic features. Ocular manifestations are similar to, but not the same as, those associated with VKC, although occasionally AKC may be a direct sequel of childhood VKC. Unlike VKC, which usually resolves spontaneously, AKC persists for many years and is associated with a high rate of significant visual morbidity. Patients with atopic dermatitis may also develop visual impairment from keratoconus, presenile cataract and rarely retinal detachment.

Clinical features

1. **The lids** are red, thickened, macerated and fissured (*see* Fig. 1.19). Associated chronic staphylococcal blepharitis is very common.

2. **Conjunctivitis** primarily involves the inferior forniceal and tarsal conjunctiva.
   - Infiltration of the tarsal conjunctiva results in an overall pale and featureless appearance (Fig. 4.45).



Fig. 4.45
Tarsal conjunctival infiltration in atopic disease

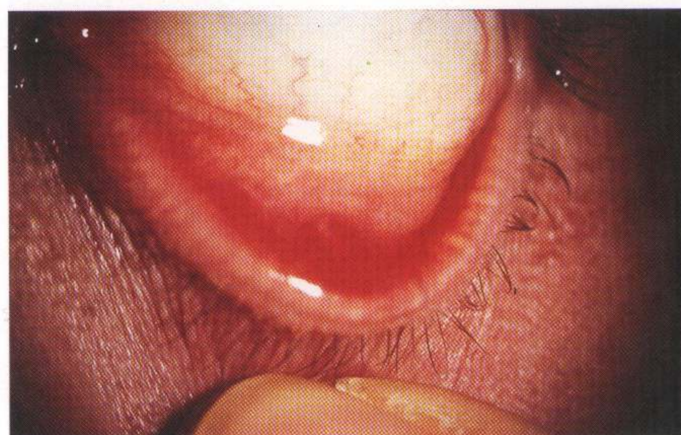


Fig. 4.46
Mild conjunctival papillary hypertrophy in atopic disease

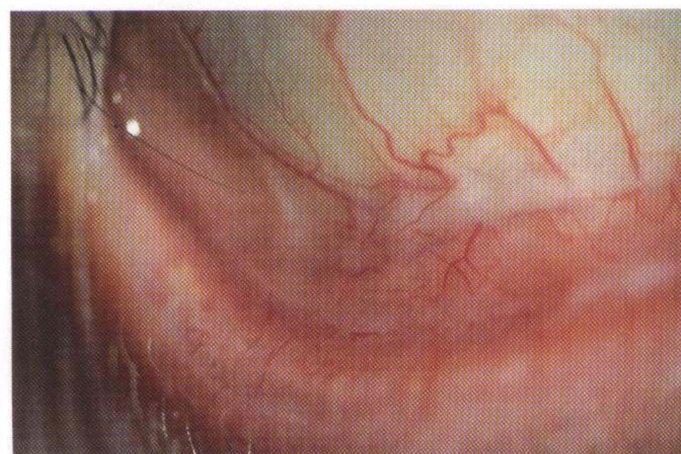


Fig. 4.47
Conjunctival scarring in advanced atopic disease

   - During exacerbations there may be chemosis, limbal hyperaemia and papillary hypertrophy (Fig. 4.46).
   - In advanced cases cicatrizing conjunctivitis may develop with inferior forniceal shortening and symblepharon formation (Fig. 4.47).
3. **Keratopathy** is the main cause of visual impairment and is characterized by the following:
   - Punctate epithelial erosions are common (Fig. 4.48).
   - More advanced lesions include persistent epithelial defects, shield-shaped anterior stromal scars (Fig. 4.49) and peripheral vascularization.
4. **Complications** include aggressive herpes simplex keratitis and microbial keratitis.

Treatment

This is similar to that of VKC but is more difficult and prolonged.

1. **Topical**
   *a. **Antibiotics*** and lid hygiene for associated staphylococcal blepharitis (*see* Chapter 1).

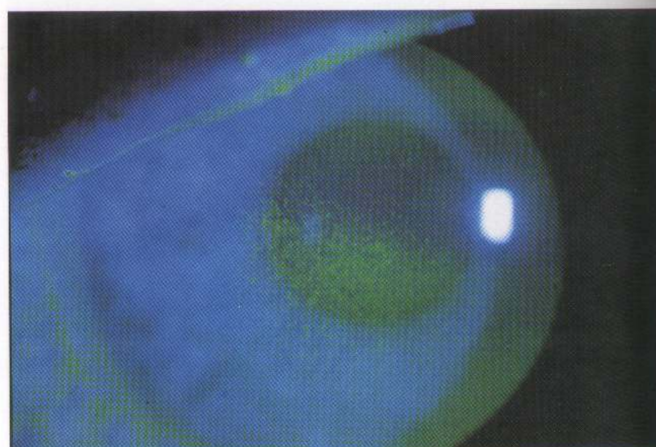


Fig. 4.48
Extensive punctate epithelial erosions in atopic disease

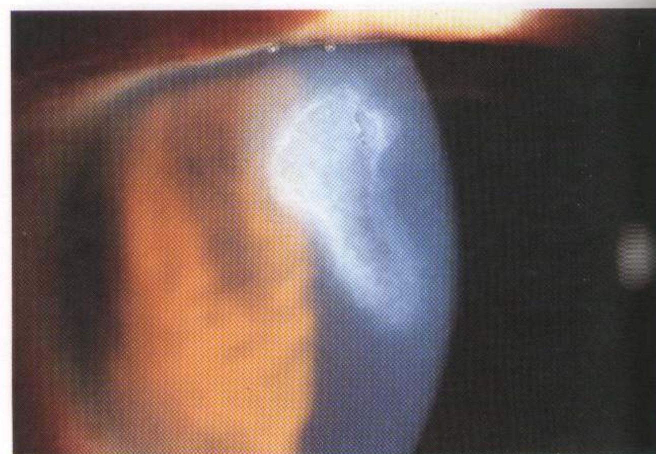


Fig. 4.49
Shield-like anterior stromal scarring in atopic disease

b. *Preservative-free lubricants* may be useful during exacerbations.

c. *Steroids* are effective as short-term treatment of severe inflammatory exacerbations and for keratopathy.

d. *Mast cell stabilizers* such as sodium cromoglycate, nedocromil and lodoxamide are effective and should be used throughout the year as prophylaxis against exacerbation and as steroid-sparing agents.

e. *Non-steroidal anti-inflammatory agents* such as ketolorac are also effective and may be used in combination with a mast cell stabilizer.

f. *Antihistamines* are less effective in AKC than in VKC.

g. *Cyclosporin 2%* is effective and safe.

2. **Supratarsal steroid injections** should be considered when topical treatment is ineffective.
3. **Systemic**

a. *Antihistamines* may be useful for severe itching.

b. *Antibiotics* such as azithromycin 500 mg once daily for 3 days may be effective in reducing inflammation aggravated by staphylococci.

c. *Cyclosporin* in severe cases.

Blistering mucocutaneous diseases

Cicatricial pemphigoid

Cicatricial pemphigoid is an idiopathic, subepidermal/subepithelial blistering and scarring autoimmune (type 2 hypersensitivity) disease characterized by autoantibodies that bind to basement membrane. The condition usually presents in late middle age and affects women more commonly than men (*see* Chapter 20). Conjunctival involvement (ocular cicatricial pemphigoid) commonly occurs in association with mucocutaneous lesions but occasionally may occur in isolation (pure ocular cicatricial pemphigoid). Ocular involvement is always bilateral, but frequently asymmetrical with regard to time of onset, severity and rate of progression.

Clinical features

1. **Presentation** is with an insidious onset of non-specific symptoms such as irritation, burning and tearing, so that the correct diagnosis may be easily overlooked.
2. **Signs** (in chronological order)
   - Papillary conjunctivitis associated with diffuse conjunctival hyperaemia.
   - Subconjunctival bullae may form and, on bursting, give rise to ulceration and the formation of pseudomembranes.
   - Subepithelial fibrosis, conjunctival shrinkage and flattening of the contour of the plica and caruncle (Fig. 4.50).

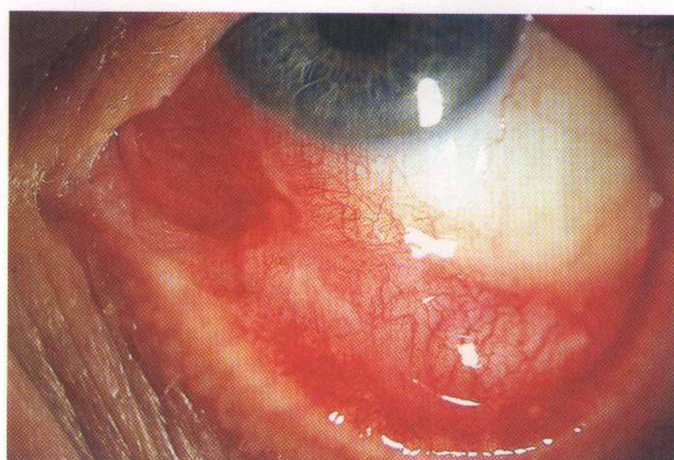


Fig. 4.50
Subconjunctival fibrosis and flattening of the plica in ocular cicatricial pemphigoid



Fig. 4.51
Active ocular cicatricial pemphigoid

- The usually progressive course of the disease may be interrupted by episodes of subacute activity, characterized by diffuse conjunctival hyperaemia and oedema (Fig. 4.51).

Complications

1. **Dry eye** is caused by a combination of destruction of goblet cells and accessory lacrimal glands as well as occlusion of the main lacrimal ductules and meibomian gland orifices.
2. **Symblepharon** is a serious complication in which adhesions form between palpebral and bulbar conjunctiva. It is best seen early in the disease process by drawing the lower eyelid down and asking the patient to look up (Fig. 4.52).
3. **Ankyloblepharon** is characterized by the formation of adhesions at the outer canthi between the upper and lower eyelids (Fig. 4.53).
4. **Secondary keratopathy**, which may be sight-threatening, is caused by a combination of entropion due

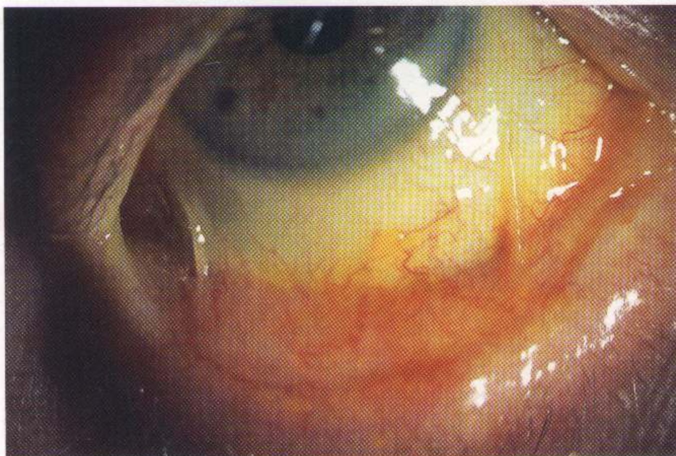

Fig. 4.52
Symblepharon in ocular cicatricial pemphigoid


Fig. 4.55
Total obliteration of the fornices in ocular cicatricial pemphigoid


Fig. 4.53
Ankyloblepharon in ocular cicatricial pemphigoid


Fig. 4.56
Secondary bacterial keratitis in ocular cicatricial pemphigoid


Fig. 4.54
Total corneal keratinization in ocular cicatricial pemphigoid

to cicatrization of palpebral conjunctiva, metaplastic lashes (*see* Fig. 1.11), lagophthalmos secondary to symblepharon, dryness and limbal stem cell depletion.

5. **End-stage disease** is characterized by keratinization of the corneal surface (Fig. 4.54), obliteration of the fornices (Fig. 4.55), corneal vascularization and ulceration which may result in secondary bacterial infection (Fig. 4.56).

Treatment

1. **Topical**
   a. *Steroids* may be beneficial during the acute stage.
   b. *Tear substitutes* may be required to alleviate tear deficiency.
   c. *Antibiotics* should be used after cultures of the conjunctiva and lids have been taken.
2. **Subconjunctival mitomycin C** injection may be effective in preventing progressive conjunctival cicatrization.
3. **Silicone contact lenses** may be used with caution to protect the cornea from aberrant lashes and drying. Rigid scleral contact lenses may be effective in holding a tear film in front of the cornea and protecting it from lid friction and exposure, but do not prevent forniceal cicatrization.
4. **Systemic** treatment is required in the majority of cases.

a. Steroids are useful for the acute manifestations.
b. Dapsone may be useful for mild to moderate involvement.
c. Cytotoxic agents (methotrexate, cyclophosphamide) may be useful in suppressing conjunctival inflammatory activity and preventing progressive conjunctival shrinkage. Azathioprine is less effective when used alone but it may be of value when added to a partially effective agent.
d. Intravenous immunoglobulin therapy may be effective for resistant cases.

5. **Surgery** may be required for the following complications:
   - Cicatricial entropion and metaplastic lashes.
   - Severe dry eyes may require punctal occlusion if the puncta have not already been occluded by scarring.
   - Large, recurrent, corneal defects may require tarsorrhaphy or injection of botulinum toxin into the levator to induce ptosis to promote healing.
   - Keratoprostheses (*see* Chapter 5) may be beneficial in eyes with advanced keratinization of the ocular surface.

Stevens–Johnson syndrome

Stevens–Johnson syndrome is an acute, severe, mucocutaneous blistering disease, which primarily occurs in young healthy individuals. Males are affected more often than females. The exact aetiology is unknown, but an abnormal immunological reaction is the probable cause. The most common precipitating factor is hypersensitivity to drugs or viral infections. The basic lesion is an acute vasculitis which affects skin and mucous membranes in all patients and the conjunctiva in 90%. The disease is self-limiting, so that when the acute phase is controlled most patients recover with good function of affected tissues (*see* Chapter 20).

Clinical features

1. **Presentation** is with fever, malaise, sore throat, and possibly cough and arthralgia which may last up to 14 days.
2. **Signs**
   - Crusty eyelids associated with a transient, self-limiting papillary conjunctivitis is the most common feature (Fig. 4.57).
   - Severe membranous or pseudomembranous conjunctivitis with patchy conjunctival infarction and the development of focal fibrotic areas is less common (Fig. 4.58).

NB: Following the acute phase of the disease, no further scarring occurs.

Complications

1. **Symblepharon** formation and keratinization.
2. **Epiphora** caused by punctal obstruction.



Fig. 4.57
Acute conjunctivitis in Stevens–Johnson syndrome

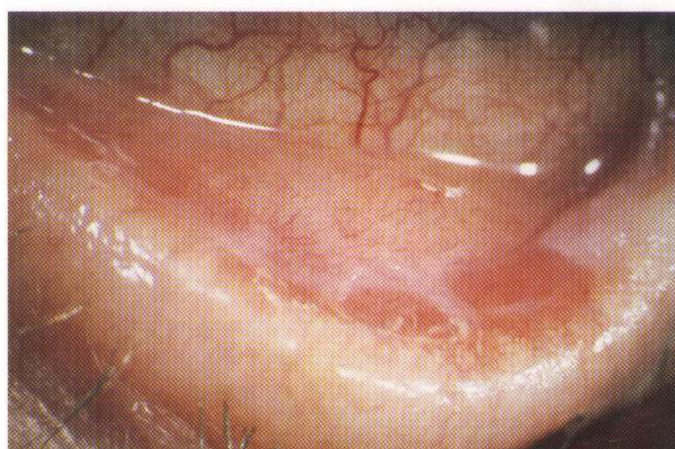


Fig. 4.58
Residual focal conjunctival fibrosis in Stevens–Johnson syndrome

3. **Dry eye** resulting from obstruction of lacrimal gland ductules.
4. **Keratopathy** secondary to cicatricial entropion, aberrant lashes and conjunctival keratinization.

Treatment

1. **Systemic** steroids are usually necessary. Aciclovir is indicated if herpes simplex is suspected as causative.
2. **Topical steroids** administered early during the course of the disease may control vasculitis and prevent conjunctival infarction.
3. **A scleral ring**, consisting of a large haptic lens with the central zone removed, may be successful in preventing symblepharon formation during the acute stage of the disease.
4. **Other measures** include the use of topical retinoic acid for keratinization, tear supplements, therapeutic contact lenses, punctal occlusion and surgery to correct permanent deformities.

Miscellaneous inflammations

Superior limbic keratoconjunctivitis

Superior limbic keratoconjunctivitis (SLK) of Theodore is an uncommon, chronic inflammatory disorder which typically affects middle-aged women who may have associated thyroid dysfunction. SLK is frequently misdiagnosed because symptoms are more severe than signs. The condition is usually bilateral, although involvement may be asymmetrical. The course is prolonged, with remissions and exacerbations until eventual resolution occurs without sequelae.

Clinical features

1. **Presentation** is with non-specific symptoms such as foreign body sensation, burning, photophobia and mucoid discharge.

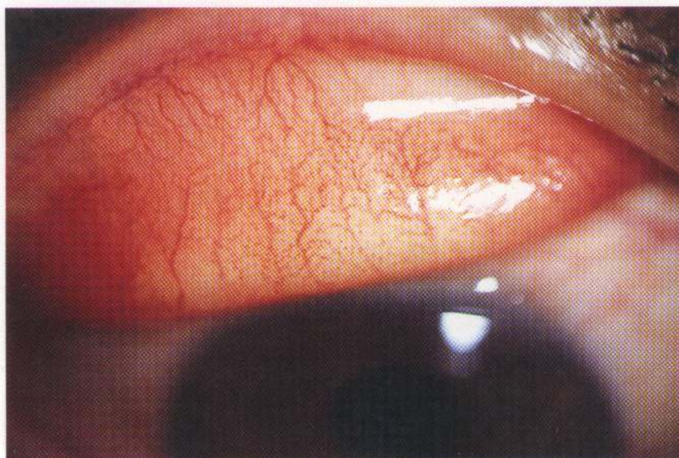


Fig. 4.59
Papillary hypertrophy in superior limbic keratoconjunctivitis

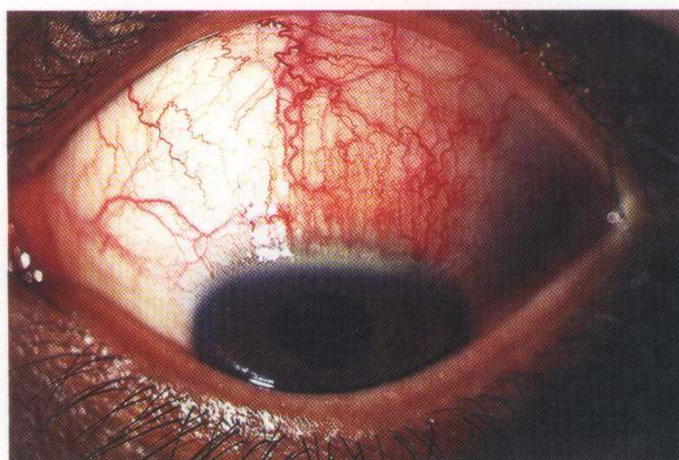


Fig. 4.60
Bulbar conjunctival hyperaemia and limbal papillary hypertrophy in superior limbic keratoconjunctivitis

2. **Signs**
   - Papillary hypertrophy of the superior tarsus which may give rise to a diffuse velvety appearance (Fig. 4.59).
   - Hyperaemia of the superior bulbar conjunctiva, which is most intense at the limbus and fades towards the superior fornix, and superior limbic papillary hypertrophy (Fig. 4.60). The conjunctival epithelial cells may become keratinized and the affected area may lack lustre.
   - Superior punctate epithelial erosions are common.
   - Superior filamentary keratitis occurs in about one-third of cases and is not necessarily associated with aqueous tear deficiency.
   - Keratoconjunctivitis sicca is present in about 25% of cases.

Treatment

This is aimed primarily at altering the abnormal mechanical interaction between the upper lid and the superior limbus. Although there is no definitive treatment, the following options are available:

1. **Tear substitutes** for associated dryness.
2. **Acetylcysteine** 5% may be helpful for filamentary keratitis.
3. **Occlusion of the upper puncta** is simple and usually effective.
4. **Soft contact lenses**, which intervene between the lid and the limbus, may be useful.
5. **Thermocauterization** of the superior bulbar conjunctiva is safe and often effective.
6. **Resection** of the superior limbal conjunctiva may help in resistant disease.

Parinaud oculoglandular syndrome

Parinaud oculoglandular syndrome is a rare condition which is most frequently caused by: (a) *cat-scratch disease* (see Chapter 20) and (b) *tularaemia*. Other causes include sporotrichosis, tuberculosis, syphilis, lymphogranuloma venereum and infectious mononucleosis as well as certain fungal, viral and rickettsial infections.

1. **Presentation** is with unilateral conjunctivitis and constitutional upset.
2. **Signs**. Unilateral granulomatous conjunctivitis with nodular elevations surrounded by follicles (Fig. 4.61), associated with severe and painful ipsilateral lymphadenopathy.
3. **Treatment** varies according to the cause. Cat-scratch disease responds to oral ciprofloxacin and co-trimoxazole.

Ligneous conjunctivitis

Ligneous conjunctivitis is a very rare disorder characterized by recurrent pseudomembranous lesions which may also

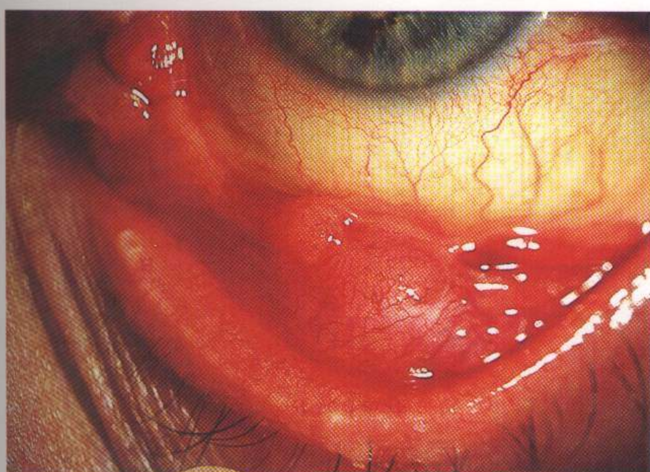


Fig. 4.61
Conjunctival granulomas and follicles in Parinaud oculoglandular syndrome



Fig. 4.62
Ligneous conjunctivitis (Courtesy of C. Barry)

involve the mouth, nasopharynx, trachea and vagina. Occasionally membrane formation may be triggered by minor trauma.

1. **Presentation** is in childhood with gradual onset of bilateral conjunctivitis which becomes chronic.
2. **Signs**. Wood-like pseudomembranous lesions of the tarsal conjunctiva (Fig. 4.62).
3. **Treatment** with topical cyclosporin is most effective. Other treatment modalities that have been tried with limited success include topical hyaluronidase, antibiotics, steroids, sodium cromoglycate and silver nitrate. Cryotherapy and surgical resection usually result in rapid recurrence.

Mucus fishing syndrome

The most frequent underlying disease which initiates the cycle of mucus fishing is keratoconjunctivitis sicca, although any condition that causes excess mucus production may be responsible. While trying to remove the excess mucus from the conjunctival sac, the patient traumatizes the conjunctival epithelium. This further increases mucus secretion, creating a vicious cycle. Mucus fishing should be suspected when appropriate treatment of an external ocular disease does not produce the expected result. On direct questioning, the patient may deny mucus fishing.

1. **Presentation** is usually in adult life with chronic mucoid discharge.
2. **Signs**. Isolated, well-circumscribed areas which stain heavily with rose bengal. Staining is usually maximal over the caruncle, plica, nasal and inferior bulbar conjunctivae, and inferior tarsal conjunctiva.
3. **Treatment** is of the underlying disorder responsible for excess mucus production. The patient should also be instructed not to touch or to attempt directly to remove mucus from the eye.

Toxic conjunctivitis

Over-the-counter non-prescription eye decongestants may be used as self medication for ocular redness and discomfort. Commonly used preparations may contain vascoconstrictors (e.g. naphazoline and phenylephrine) with or without antihistamines. If used inappropriately they may give rise to conjunctivitis with irritation, burning, foreign body sensation and redness. The diagnosis is made by exclusion after other causes of conjunctivitis have been considered. The patient who does not recognize cause and effect may not volunteer the information.

1. **Signs**
   a. ***Diffuse conjunctival hyperaemia***, the most frequent, is probably a rebound phenomenon following discontinuation of a vasoconstrictor, similar to that occurring with nasal preparations. The hyperaemia is associated with papillae on the upper (Fig. 4.63) and lower tarsal conjunctiva.
   b. ***Follicular conjunctivitis***, probably due to a toxic effect, is less common and is most prominent on the inferior forniceal conjunctiva (Fig. 4.64).
   c. ***Blepharoconjunctivitis***, due to hypersensitivity, is the least common and is characterized by oedema and hyperaemia of the lids and conjunctiva.

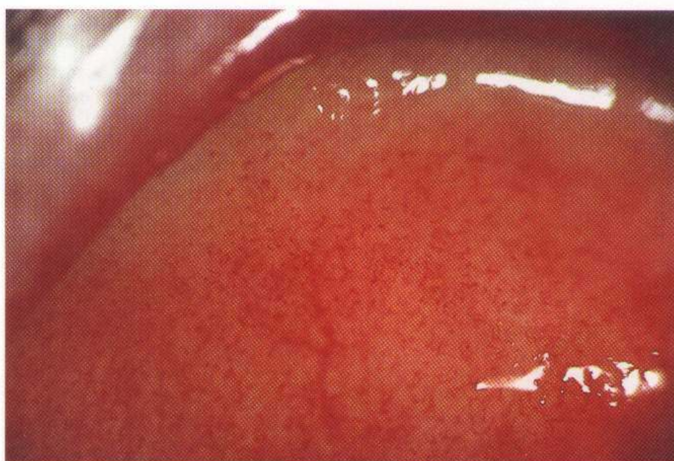


Fig. 4.63
Toxic papillary conjunctivitis

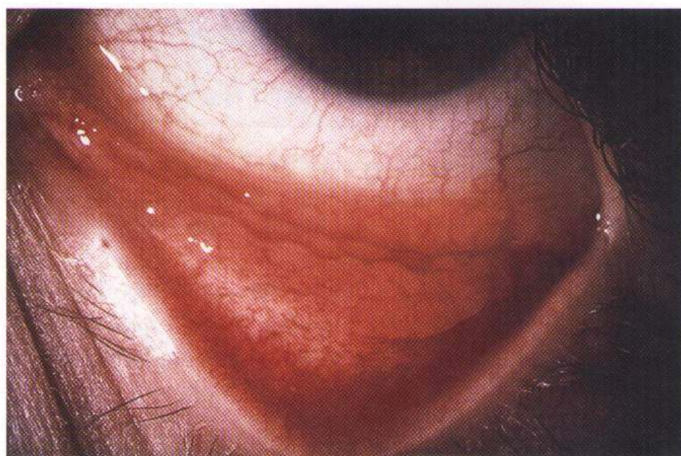


Fig. 4.64
Toxic follicular conjunctivitis

2. **Treatment** involves discontinuation of topical medication. It must be explained that symptoms may temporarily worsen and then improve. Follicular conjunctivitis may take many weeks to resolve, particularly if the drops have been used for a long time. In such cases topical steroids may shorten recovery time. Blepharoconjunctivitis may also respond to a short course of topical steroids.

Degenerations

Pinguecula

Pinguecula is an extremely common, innocuous, usually bilateral and asymptomatic condition.

1. **Signs**. Yellow-white deposits on the bulbar conjunctiva adjacent to the nasal or temporal limbus (Fig. 4.65).
2. **Treatment** is usually unnecessary because growth is very slow or absent. Occasionally, however, a pinguecula may become acutely inflamed (pingueculitis) and require a short course of a weak steroid such as fluorometholone.

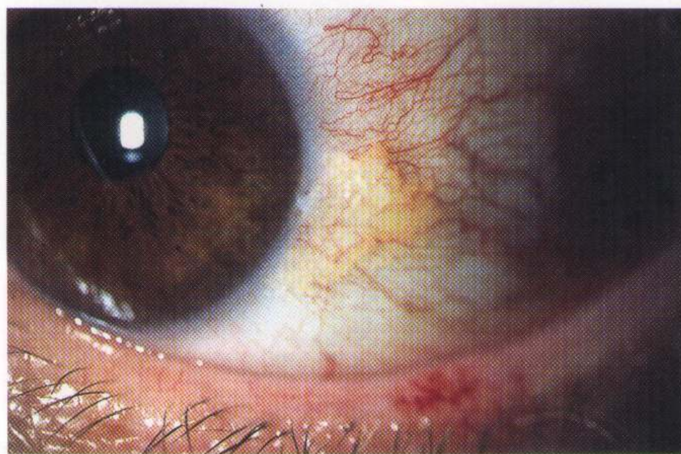


Fig. 4.65
Pinguecula

Pterygium

A pterygium is a triangular fibrovascular subepithelial ingrowth of degenerative bulbar conjunctival tissue over the limbus onto the cornea. Pterygia typically develop in patients who have been living in hot climates and may represent a response to chronic dryness and ultraviolet exposure.

Clinical features

1. **Signs** (in chronological order)
   - A small, grey, corneal opacity develops near the nasal limbus (Fig. 4.66).
   - The conjunctiva overgrows the opacity and progressively encroaches onto the cornea in a triangular fashion (Figs 4.67, 4.68).
   - A deposit of iron (Stocker line) may be seen in the corneal epithelium anterior to the advancing head of the pterygium.

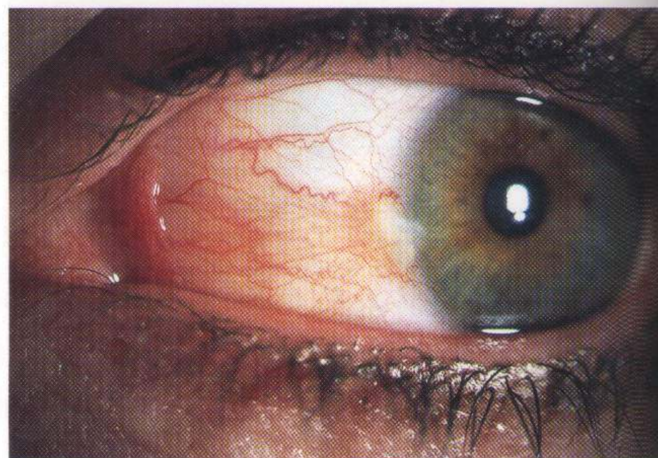


Fig. 4.66
Early pterygium

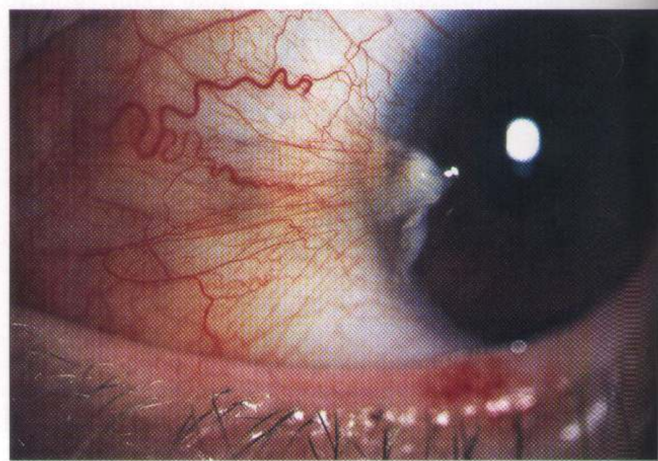


Fig. 4.67
Established pterygium

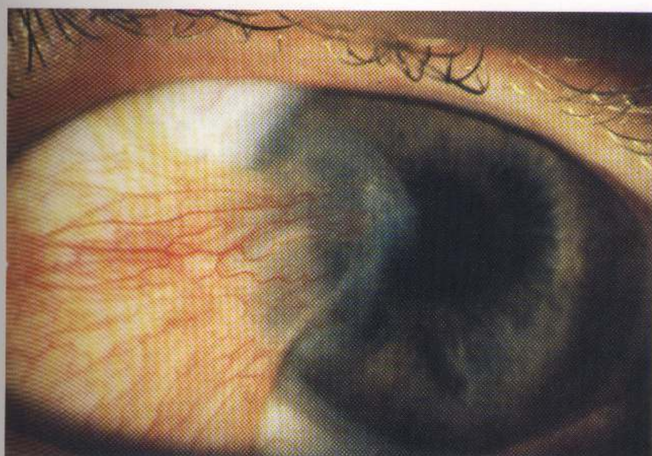


Fig. 4.68
Advanced pterygium



Fig. 4.69
Pterygium involving the visual axis

2. **Complications** include chronic irritation, decreased vision due to involvement of the visual axis (Fig. 4.69) or induced astigmatism, and disruption of the pre-corneal tear film. A pterygium may become intermittently inflamed and require a short course of a weak topical steroid.

Treatment

This is indicated either for cosmetic reasons or occasionally progression towards the visual axis. Simple excision is associated with a high rate of recurrence, frequently more aggressive than the initial lesion. Numerous techniques aimed at preventing recurrence have been described. Currently the most widely used technique involves excision of the pterygium and covering of the defect with either a conjunctival autograft or amniotic membrane. Adjunctive treatment with mitomycin C and beta-irradiation may be used to minimize recurrence but may rarely be complicated by late scleral necrosis.

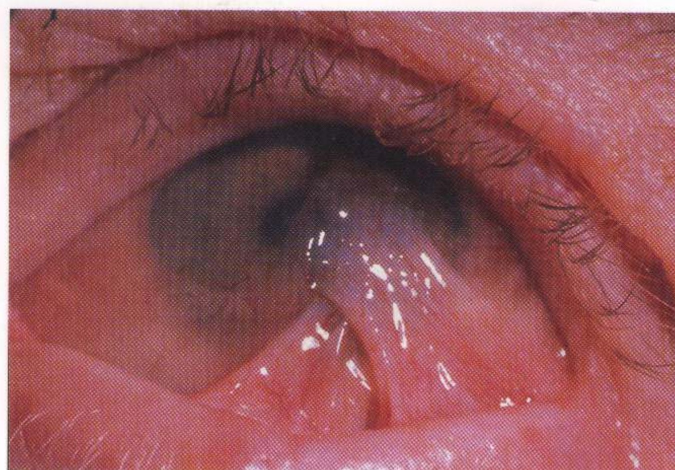


Fig. 4.70
Pseudopterygium

Differential diagnosis

1. **A pseudopterygium** is caused by the adhesion of a fold of conjunctiva to a peripheral corneal ulcer or area of peripheral thinning, and is fixed only at its apex to the cornea (Fig. 4.70). A true pterygium is adherent to underlying structures throughout.
2. **Conjunctival intraepithelial neoplasia** (*see* below).

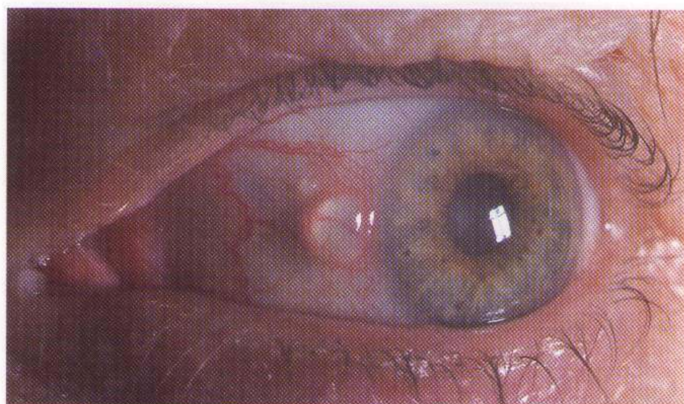
Concretions

Concretions are extremly common lesions which most frequently affect elderly patients and may also occur in chronic meibomian gland disease.

1. **Signs**. Small, often multiple, chalky, yellow-white deposits most commonly seen in the inferior tarsal and forniceal conjunctiva (Fig. 4.71).
2. **Treatment** is usually unnecessary because concretions are subepithelial and asymptomatic. If a large concretion erodes through the epithelium and causes irritation



Fig. 4.71
Conjunctival concretions


Fig. 4.72
Conjunctival retention cyst

it can be removed under topical anaesthesia with a needle.

Retention cyst

A retention cyst is a very common, usually asymptomatic, thin-walled lesion containing clear fluid (Fig. 4.72). Treatment, if appropriate, is by simple puncture with a needle.

Pigmented lesions

Conjunctival epithelial melanosis

Conjunctival (racial) epithelial melanosis is a benign condition often seen in dark-skinned individuals. Both eyes are affected but the intensity may be asymmetrical.

1. **Presentation** is during the first few years of life. The melanosis becomes static by early adulthood.


Fig. 4.73
Conjunctival epithelial melanosis

2. **Signs**
   - Areas of flat, patchy, brownish pigmentation scattered throughout the conjunctiva (Fig. 4.73).
   - With the slit-lamp the pigmentation is seen to be within the epithelium and therefore moves freely over the surface of the globe.
   - The lesions may be more intense at the limbus and around the perforating branches of the anterior ciliary vessels as they enter the sclera.
   - Juxtalimbal pigmentation may extend onto the peripheral cornea.
3. **Differential diagnosis**
   a. ***Conjunctival freckle*** is a tiny area of epithelial pigmentation (Fig. 4.74).
   b. ***Axenfeld loop*** is an area of melanosis around an intrascleral nerve or an anterior ciliary artery (Fig. 4.75).
   c. ***Mascara deposits*** usually accumulate in the inferior fornix (Fig. 4.76).
   d. ***Adrenochrome*** deposits are tiny clumps of pigment on the tarsal or forniceal conjunctiva associated with the


Fig. 4.74
Conjunctival freckle


Fig. 4.75
Melanosis around an intrascleral nerve

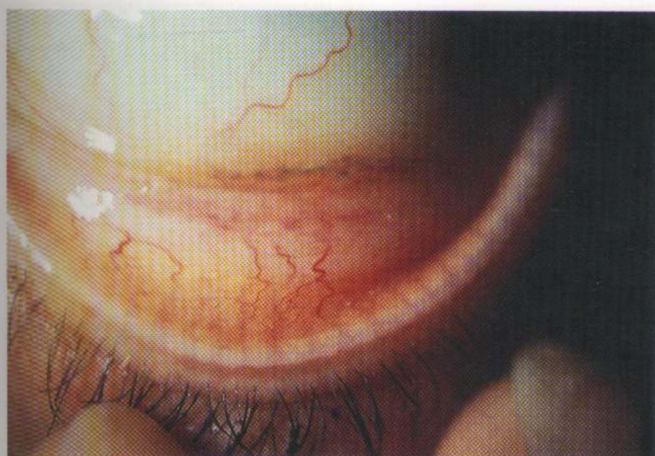


Fig. 4.76
Forniceal mascara deposits



Fig. 4.77
Conjunctival adrenochrome deposits

long-term use of adrenaline drops for glaucoma (Fig. 4.77).

Congenital ocular melanocytosis

Classification

Congenital ocular melanocytosis is an uncommon melanocytic hyperplasia which occurs in three clinical settings:

1. **Ocular melanocytosis**, the least common, involves only the eye.
2. **Dermal melanocytosis** involves only the skin and accounts for about one-third of cases.
3. **Oculodermal melanocytosis** (naevus of Ota) involves both skin and eye. It is the most frequently encountered type.

Clinical features

1. **Signs**
   - Multifocal, slate-grey pigmentation which lies subconjunctivally in the episclera and cannot be moved over the globe (Fig. 4.78).
   - Occasionally the peripheral cornea may be involved.

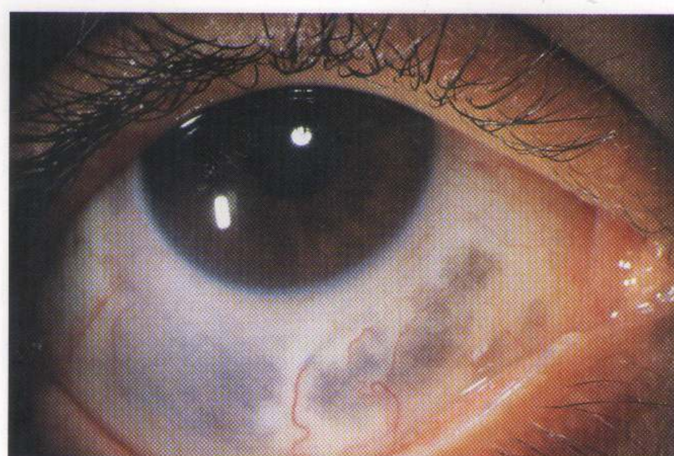


Fig. 4.78
Congenital subepithelial melanocytosis (Courtesy of B. Jay)

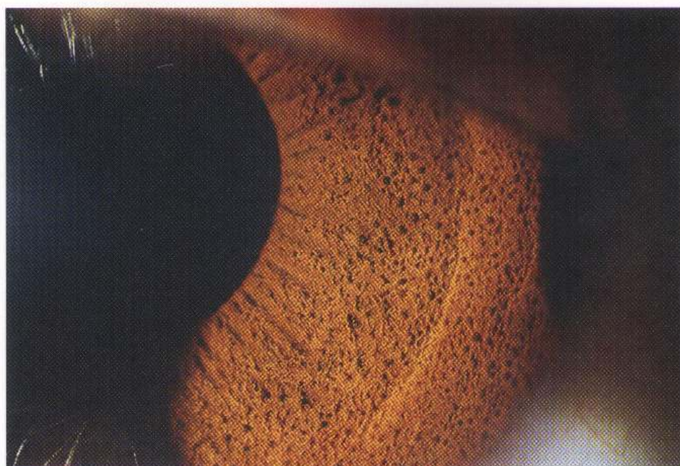


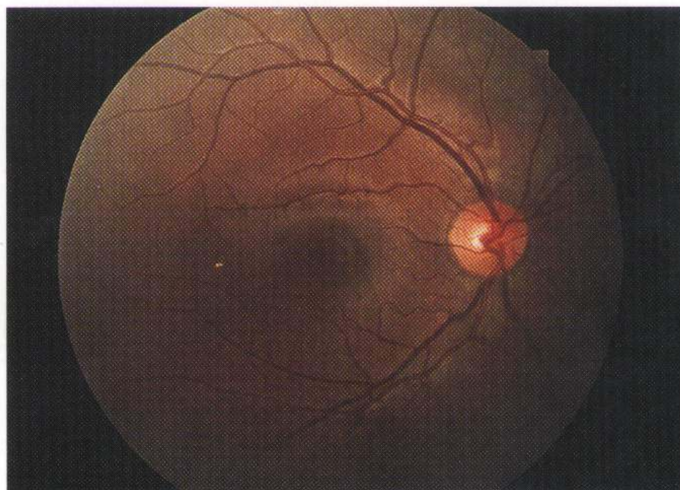
Fig. 4.79
Right congenital dermal melanocytosis in naevus of Ota

2. **Naevus of Ota**
   - Unilateral deep hyperpigmentation of facial skin, most frequently in the distribution of the first and second divisions of the trigeminal nerve (Fig. 4.79). It may be subtle in fair-skinned individuals and is best detected by observation in good lighting.
   - Involvement of the third division of the trigeminal nerve and of the nasal and buccal mucosa is uncommon.



Fig. 4.80
Right congenital conjunctival subepithelial melanocytosis and right iris hyperchromia in naevus of Ota


Fig. 4.81
Iris mammillations in naevus of Ota

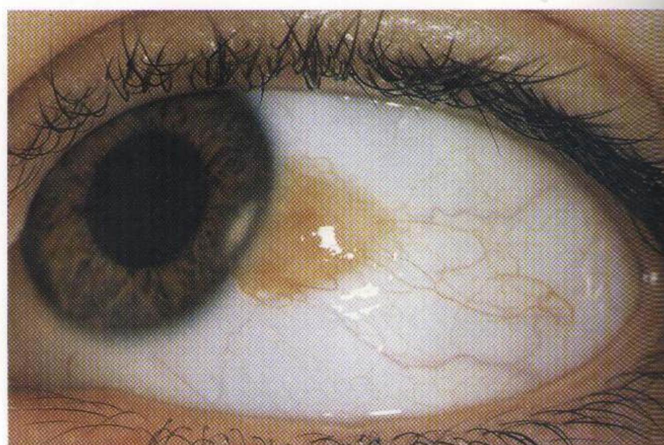

Fig. 4.82
Fundus hyperpigmentation in naevus of Ota

Ipsilateral associations

1. **Iris hyperchromia** is common (Fig. 4.80).
2. **Iris mammillations**, which are tiny, regularly spaced, villiform lesions, are uncommon (Fig. 4.81). They may also be found in patients with neurofibromatosis-1, Axenfeld–Rieger anomaly and Peters anomaly.
3. **Fundus hyperpigmentation** is uncommon (Fig. 4.82).
4. **Melanoma** of the uveal tract, orbit, optic nerve head or brain may develop in a minority of white people.
5. **Glaucoma**, associated with trabecular hyperpigmentation, develops in about 10% of cases.

Conjunctival naevus

A conjunctival naevus is a relatively uncommon, benign, usually unilateral condition. The most common location is the juxtalimbal area (Fig. 4.83), followed by the plica and caruncle (Fig. 4.84).


Fig. 4.83
Non-pigmented conjunctival naevus

1. **Presentation** is usually during the first two decades of life with ocular irritation or a pigmented lesion.
2. **Signs**
   - Solitary, sharply demarcated, flat or slightly elevated intraepithelial lesion which can be moved freely over the scleral surface. Cystic spaces within the naevus are frequent.
   - The extent of pigmentation is variable and some may be virtually non-pigmented (*see* Fig. 4.83).
   - Pigmented naevi virtually always contain some shade of brown, ranging from tan to deep chocolate (Fig. 4.85).
   - Around puberty the naevus may enlarge and become more pigmented.
3. **Signs of potential malignancy**
   - An unusual site such as palpebral or forniceal conjunctiva.
   - Extension onto the cornea.
   - Sudden increase in pigmentation or growth.
   - Development of vascularity except at puberty.
4. **Treatment** by excision is indicated mainly for cosmetic reasons. Less common indications include irritation and suspicion of malignant transformation.


Fig. 4.84
Caruncular naevus


Fig. 4.85
Pigmented conjunctival naevus

Primary acquired melanosis

Classification

Primary acquired melanosis (PAM) is an uncommon, almost always unilateral condition which typically affects middle-aged white people. The two histological types are as follows:

1. **PAM without atypia** is a benign proliferation of normal melanocytes, confined to the basal layer of the conjunctiva.
2. **PAM with atypia** is a pre-malignant condition with a 50% chance of malignant transformation within 5 years. It is characterized by an increase in number of large melanocytes with prominent nucleoli, involving all layers of the conjunctiva (pagetoid spread).

Clinical features

1. **Presentation** of PAM without atypia can be at any age, but PAM with atypia is usually seen after the age of 45 years.
2. **Signs**
   - Irregular, unifocal or multifocal areas of flat, brown pigmentation which may involve any part of the conjunctiva (Figs 4.86, 4.87):
   - The lesions involve the epithelium and can therefore be moved over the surface of the globe.


Fig. 4.86
Primary acquired melanosis (Courtesy of B. Jay)

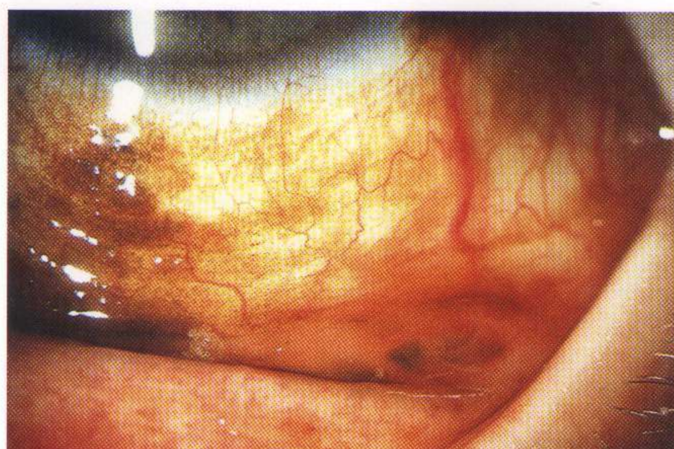

Fig. 4.87
Primary acquired melanosis


Fig. 4.88
Melanoma associated with primary acquired melanosis (Courtesy of B. Jay)

   - PAM may shrink or remain stable for long periods of time. It may also lighten, darken focally, or enlarge centrifugally (radial growth).

> *NB:* Multiple biopsies assisted by immunohistochemistry are required for diagnosis because the clinical features of PAM with and without atypia are the same. A sign of malignant transformation of PAM to melanoma is the sudden appearance of one or more nodules in otherwise flat lesions (Fig. 4.88).

Treatment

1. **PAM without atypia** does not require treatment.
2. **PAM with atypia**
   - Small areas are treated by excision.
   - Larger areas that cannot be excised may be treated with cryotherapy or by topical application of mitomycin C.

Conjunctival melanoma

Conjunctival melanoma accounts for about 2% of all ocular malignancies.

Classsification

1. **Melanoma arising from PAM with atypia** accounts for 75% of cases (Fig. 4.89).
2. **Melanoma arising from a pre-existing naevus** accounts for 20%.
3. **Primary melanoma** is the least common.

Primary melanoma

1. **Presentation** is in the sixth decade except in patients with the rare dysplastic naevus syndrome, who develop multiple melanomas earlier.
2. **Signs**
   - A solitary, black or grey nodule containing dilated feeder vessels which may become fixed to episclera (Fig. 4.90).



Fig. 4.89
Multifocal melanoma associated with primary acquired melanosis

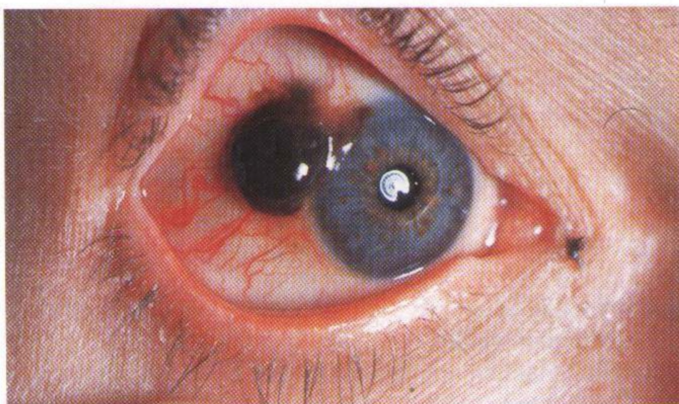


Fig. 4.90
Primary pigmented conjunctival melanoma (Courtesy of B. Jay)



Fig. 4.91
Primary amelanotic conjunctival melanoma

   - Amelanotic tumours are pink and have a characteristic, smooth, fish-flesh appearance (Fig. 4.91).
   - A common site is the limbus although the tumour may arise anywhere in the conjunctiva.

Treatment

1. **Circumscribed melanoma**
   - Surgical excision with a wide clearance and cryotherapy to prevent recurrence.
   - If histology reveals incomplete clearance, wide re-excision of the surgical scar and further cryotherapy are indicated.
   - Re-examination of the patient is at 6–12-monthly intervals for life. At each visit the entire conjunctival surface is examined and any suspicious areas examined histologically following biopsy or impression cytology.
2. **Diffuse melanoma** is treated by excision of localized nodules and cryotherapy or mitomycin C to the diffuse component (Fig. 4.92).
3. **Orbital recurrences** are treated by local resection and radiotherapy (Fig. 4.93). Exenteration does not improve



Fig. 4.92
Diffuse conjunctival melanoma


Fig. 4.93
Recurrence of conjunctival melanoma


Fig. 4.95
Conjunctival melanocytoma

the survival rate and is therefore reserved for patients with extensive and aggressive disease that cannot be controlled by other methods.

4. **Lymph node involvement** is treated by surgical excision and radiotherapy.
5. **Palliation** is with chemotherapy for metastatic disease.

Prognosis

The overall mortality is about 12% at 5 years and 25% at 10 years. The main sites for metastases are regional lymph nodes, lung, brain and liver. Poor prognostic indicators include:

- Multifocal tumours.
- Extralimbal tumours involving the caruncle, fornix or palpebral conjunctiva.
- Tumour thickness of 2 mm or more.
- Recurrence.
- Lymphatic or orbital spread.

Differential diagnosis

1. **A large naevus** that is growing during puberty (Fig. 4.94). However, unlike melanoma it does not involve the cornea.
2. **Ciliary body melanoma** with extraocular extension (*see* Fig. 11.22).
3. **Melanocytoma** is a rare, congenital, black, slow-growing lesion which cannot be moved freely over the globe (Fig. 4.95).
4. **Pigmented conjunctival carcinoma** in a dark-skinned individual.

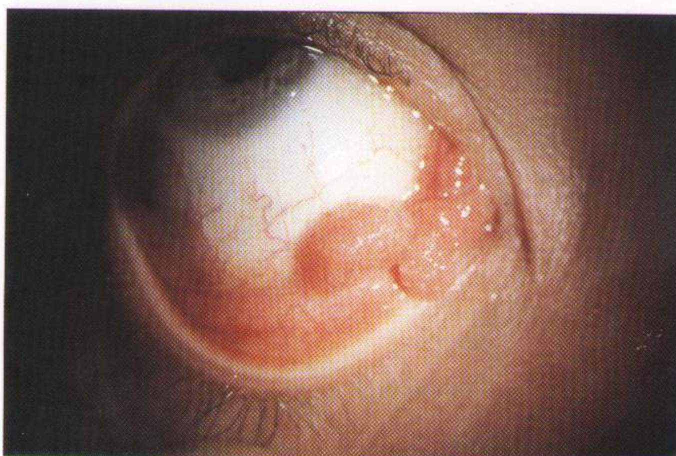
Squamous tumours

Conjunctival papilloma

Pedunculated papilloma

This is caused by infection with human papillomavirus (types 6 and 11), which may occur by mother-to-infant transmission at birth through an infected vagina.


Fig. 4.94
Large conjunctival naevus


Fig. 4.96
Pedunculated conjunctival papillomas

1. **Presentation** may be early after birth or years later.
2. **Signs**. The papillomas, which may be multiple and occasionally bilateral, are most frequently located in the palpebral conjunctiva, fornix or caruncle (Fig. 4.96).
3. **Treatment** of small lesions may not be required because they often resolve spontaneously. Large lesions are treated by excision biopsy or cryotherapy. Treatment options for recurrences include subconjunctival interferon alpha, topical mitomycin C or oral cimetidine (Tagamet).

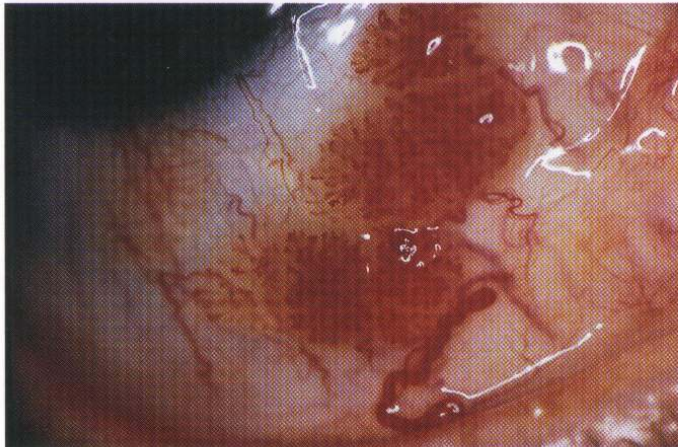


Fig. 4.97
Sessile conjunctival papilloma

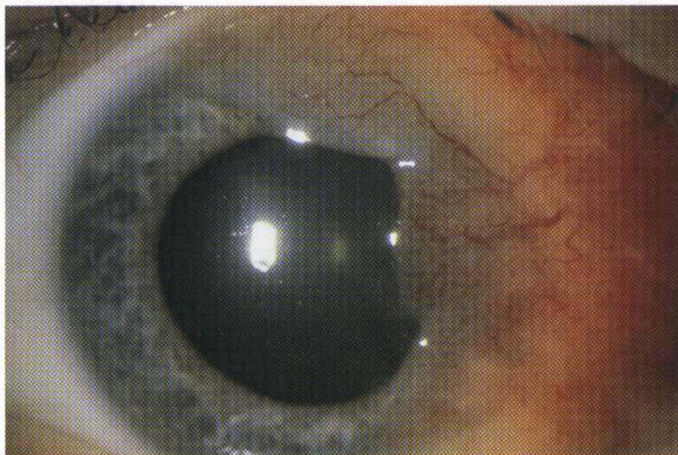


Fig. 4.98
En-plaque conjunctival intraepithelial neoplasia

Sessile papilloma

Sessile (neoplastic) papilloma is not infectious.

1. **Presentation** is usually in middle age.
2. **Signs**. The lesion is single, unilateral and most frequently located on the bulbar and juxtalimbal conjunctiva (Fig. 4.97).
3. **Treatment** is by excision.

Conjunctival and corneal intraepithelial neoplasia

Conjunctival and corneal intraepithelial neoplasia (CCIN) is an uncommon, benign, slowly progressive unilateral disease with low malignant potential. Histological changes range from mild to severe epithelial dysplasia confined to the basal third of the epithelium to full-thickness epithelial involvement with dysplastic cells (carcinoma in situ). Risk factors include ultraviolet light exposure, human papilloma virus infection and AIDS.

Clinical features

1. **Presentation** is usually in late adult life with ocular irritation or a mass.
2. **En plaque** CCIN is a raised, gelatinous or leucoplakic growth with tufts of superficial blood vessels at the limbus within the interpalpebral fissure (Fig. 4.98).
3. **Papillomatous** CCIN is a raised discrete lesion with surface corkscrew-like blood vessels (Fig. 4.99).
4. **Diffuse** CCIN, which is uncommon, is characterized by indistinct conjunctival thickening (Fig. 4.100).

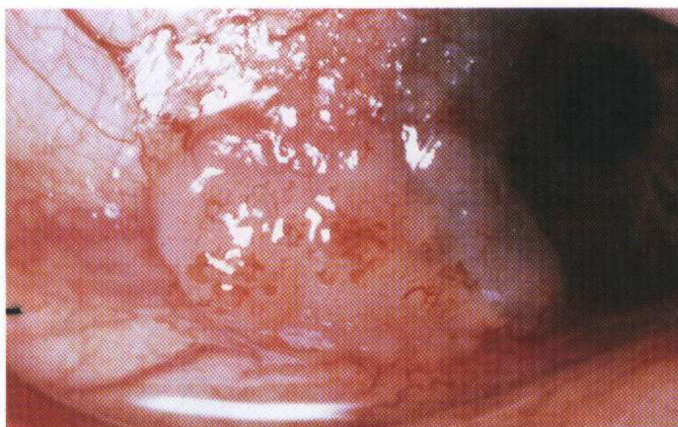


Fig. 4.99
Papillomatous conjunctival intraepithelial neoplasia (Courtesy of C. Barry)

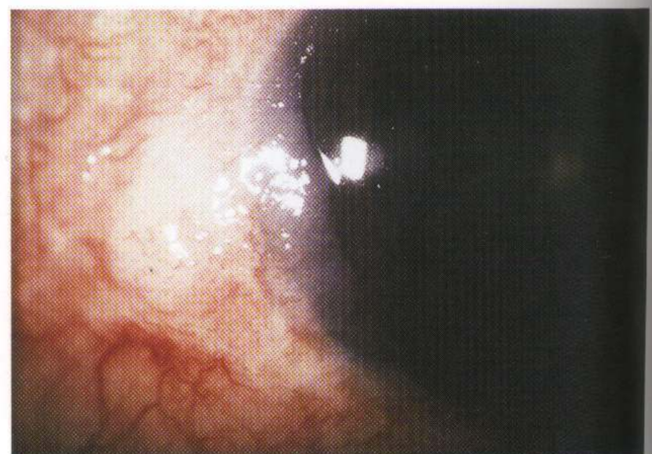


Fig. 4.100
Diffuse conjunctival intraepithelial neoplasia

NB: All three varieties may be associated with grey-white hyperplastic epithelium that extends onto the cornea. Impression cytology may be useful in diagnosis.

Treatment

1. **Localized** CCIN is treated by excision with adjunctive cryotherapy.
2. **Diffuse** CCIN is more difficult to treat because the poorly defined borders render involved tissue clinically indistinguishable from healthy tissue. This frequently results in incomplete excision and a high rate of recurrence. Other treatment modalities have therefore been introduced either as alternatives or adjuncts to surgery. These include topical mitomycin C, 5-fluorouracil and interferon alpha-2b.

Differential diagnosis

1. **Atypical conjunctival papilloma**.
2. **Pterygium**, which is also associated with exposure to ultraviolet radiation.
3. **Pseudo-epitheliomatous hyperplasia**, which is a rapidly growing, white, hyperkeratotic, juxtalimbal nodule which develops secondary to irritation (Fig. 4.101).
4. **Unilateral chronic conjunctivitis**, which may be mimicked by diffuse CCIN.
5. **Amelanotic melanoma**.
6. **Conjunctival carcinoma** (*see* below).

Conjunctival squamous cell carcinoma

Conjunctival squamous cell carcinoma is a rare, slow-growing tumour of low-grade malignancy which may arise *de novo* or from pre-existing CCIN. It occurs with increased frequency in patients with xeroderma pigmentosum and AIDS.

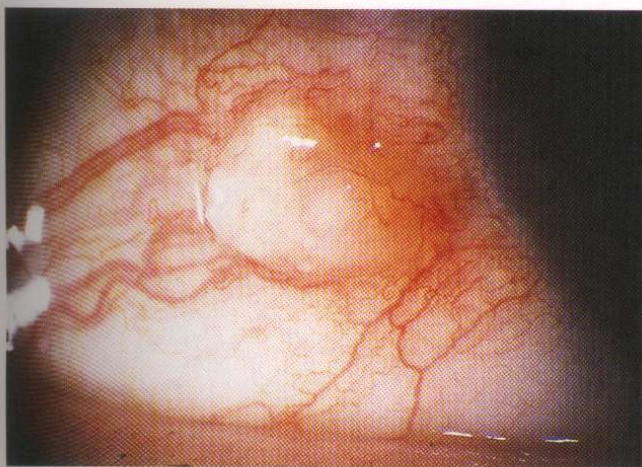


Fig. 4.101
Pseudo-epitheliomatous conjunctival hyperplasia

Clinical features

1. **Presentation** is usually in late adult life in a similar way to CCIN.
2. **Signs**
   - A fleshy, pink, papillomatous or gelatinous mass, often associated with feeder vessels (Fig. 4.102), which may sometimes be covered by plaques of keratin.
   - The tumour is most frequently juxtalimbal and seldom arises from forniceal or palpebral conjunctiva.
   - Limbal tumours may involve adjacent cornea (Fig. 4.103) but scleral (deep) invasion is uncommon.

Treatment

1. **Surgical excision** and adjunctive cryotherapy.
2. **Topical chemotherapy** with mitomycin C or 5-fluorouracil may be indicated for recurrences or primary treatment of selected early cases.
3. **Enucleation** in cases of intraocular invasion.
4. **Exenteration** for advanced cases with orbital involvement.

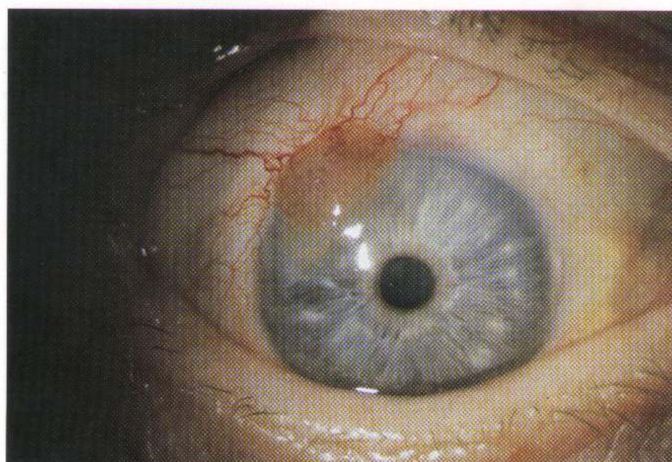


Fig. 4.102
Conjunctival squamous cell carcinoma invading the cornea



Fig. 4.103
Advanced conjunctival squamous cell carcinoma (Courtesy of C. Barry)

Miscellaneous tumours

Conjunctival sebaceous gland carcinoma

Sebaceous gland carcinoma is a very rare but aggressive tumour which may invade the orbit and metastasize to local lymph nodes as well as distant sites. It is seen in the following two clinical settings:

1. **Conjunctival intraepithelial invasion** of sebaceous gland carcinoma (pagetoid spread) from a tumour primarily involving the meibomian glands or glands of Zeis (*see* Chapter 1). In this setting it may mimic chronic blepharoconjunctivitis.
2. **Primary intraepithelial carcinoma** arising from and confined to the conjunctival epithelium is much less common (Fig. 4.104).

Epibulbar choristoma

A choristoma is a congenital overgrowth of normal tissue in an abnormal location. There are two main types: (a) *dermoids* and (b) *lipodermoids.*

Dermoid

Dermoids may occur in isolation or often in patients with Goldenhar syndrome (Fig. 4.105), Treacher Collins syndrome and naevus sebaceous syndrome of Jadassohn. Dermoids contain a variety of tissues such as cartilage, fat, muscle, hair follicles and sebaceous glands.

1. **Presentation** is in early childhood.
2. **Signs**. Smooth, soft, yellowish, subconjunctival masses most frequently located at the inferotemporal limbus (Fig. 4.106). Occasionally the lesions are very large and may virtually encircle the limbus (Fig. 4.107). Bilateral involvement is uncommon.
3. **Treatment** is indicated if the lesion causes a cosmetic deformity, extends to the visual axis, causes astigmatism

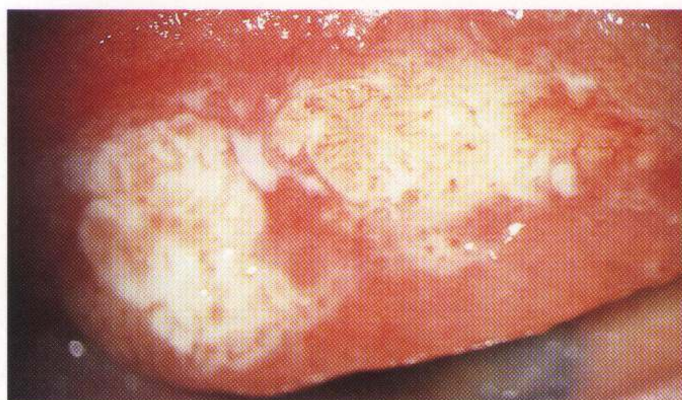


Fig. 4.104
Conjunctival intraepithelial sebaceous gland carcinoma



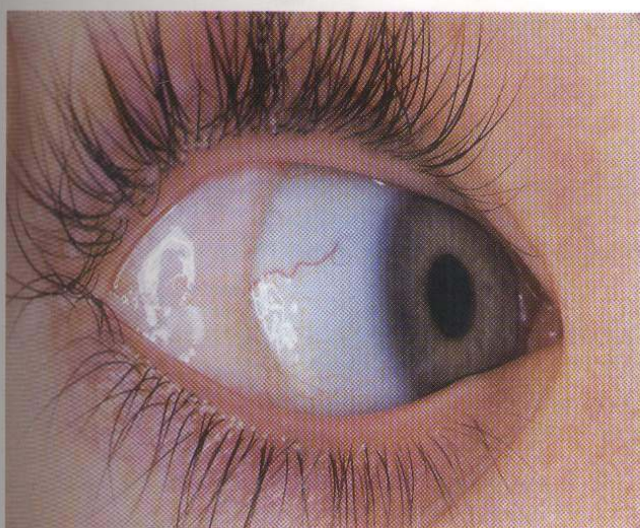
Fig. 4.106
Localized limbal dermoid



Fig. 4.105
Limbal dermoid in Goldenhar syndrome



Fig. 4.107
Large limbal dermoid


Fig. 4.108
Lipodermoid

or dellen formation, or chronic ocular irritation. Small lesions can be excised although the removal of large lesions may be more complicated and may require lamellar corneal or scleral grafting.

Lipodermoid

1. **Presentation** is in adult life.
2. **Signs**. Soft, movable, subconjunctival mass most commonly located at the outer canthus (Fig. 4.108).
3. **Treatment** should be avoided because surgery may be complicated by scarring, ptosis, dry eye and ocular motility problems. However, if they are particularly unsightly, then debulking the anterior portion may improve cosmesis without compromising ocular motility.

Conjunctival lymphoma

Lymphocytes normally reside in the substantia propria, so that the conjunctiva, similar to extranodal lymphoid sites such as the bowel and lung, may be the seat of lymphoproliferative lesions that constitute a spectrum ranging from benign reactive hyperplasia through atypical hyperplasia to lymphoma. Benign and malignant lesions share similar characteristics and cannot be differentiated clinically. Occasionally reactive hyperplasia undergoes malignant transformation to lymphoma. Most conjunctival lymphomas are of B-cell origin with systemic involvement in about 30% of cases.

1. **Presentation** is usually in late adult life with irritation or painless swelling.
2. **Signs**. Slow-growing, mobile, salmon-pink or flesh-coloured infiltrates in the inferior fornices or epibulbar surfaces which may be bilateral (Fig. 4.109). The lesions may be localized to the conjunctiva or associated with orbital involvement.

> *NB:* Rarely a diffuse lymphoma may mimic chronic conjunctivitis (Fig. 4.110).

3. **Treatment** is most frequently with radiotherapy. Other options include chemotherapy, excision, cryotherapy and local injection of interferon alpha-2b.

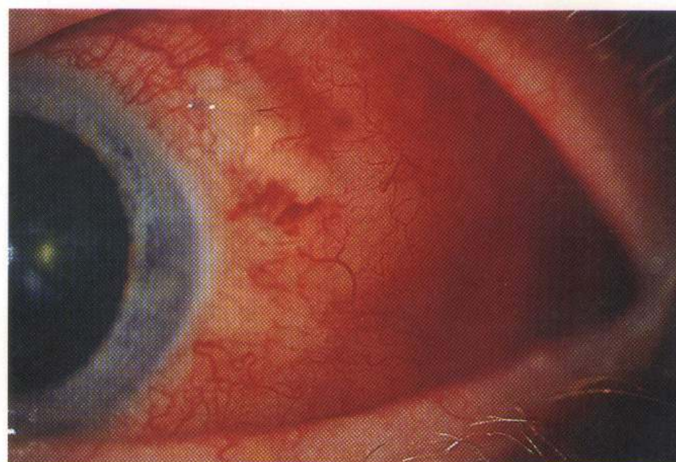
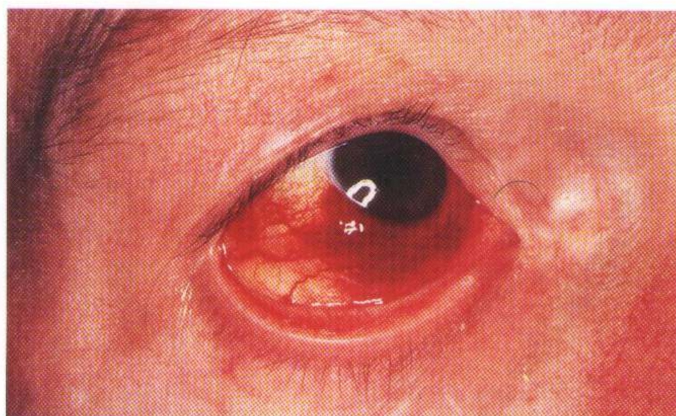

Fig. 4.110
Conjunctival lymphoma mimicking chronic conjunctivitis


Fig. 4.109
Conjunctival lymphoma


Fig. 4.111
Conjunctival Kaposi sarcoma

Conjunctival Kaposi sarcoma

Kaposi sarcoma is a slow-growing, low-grade malignancy which occurs in patients with AIDS.



Fig. 4.112
Conjunctival pyogenic granuloma

1. **Presentation** is in adult life with irritation or painless discoloration.
2. **Signs**. A flat, bright-red lesion, most often located in the inferior fornix which may be mistaken for a 'chronic' subconjunctival haemorrhage (Fig. 4.111).
3. **Treatment** is required for cosmetic reasons, bleeding or infection. Options include focal radiotherapy and excision with or without adjunctive cryotherapy.

Conjunctival pyogenic granuloma

A pyogenic granuloma is a vascularized proliferation of granulomatous tissue.

1. **Presentation** is frequently a few weeks after conjunctival surgery such as excision of a pterygium.
2. **Signs**. A fleshy, vascularized conjunctival mass (Fig. 4.112).
3. **Treatment** is by excision.